Apparatus and containers for performing polymerase chain reaction

Patent Number:	EP0810030
Publication date:	1997-12-03
Inventor(s):	ATWOOD JOHN GIRDNER (US); LEATH RICHARD (US); GOVEN LISA MAY (US); RAGUSA ROBERT P (US); WILLIAMS FENTON (US); MARGULIES MARCEL (US); MOSSA ALBERT CARMELO (US); WOUDENBERG TIMOTHY M (US)
Applicant(s):	PERKIN ELMER CORP (US)
Requested Patent:	☐ EP0810030
Application Number:	EP19970112541 19911129
Priority Number (s):	EP19910311090 19911129; US19900620606 19901129; US19910670545 19910314
IPC Classification:	B01L7/00; B01L3/00; B01L9/06; C12Q1/68; G05D23/19
EC Classification:	G05D23/19D, B01L3/00C2D2, B01L3/00C2D4, B01L7/00, B01L7/00D, G05D23/19E
Equivalents:	☐ EP0812621, B1

Abstract

A thermocycler apparatus for performing polymerase chain reaction (PCR) comprises a heating block (12) and heated cover (14) in which sample tubes (324,326) are retained, heated and cooled as required. The heating of the upper portions and caps of sample tubes (324,326) in use prevents condensation inside the tube caps thereby eliminating the need for a layer of oil floating on the surface of the sample liquid.

(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) EP 0 810 030 A1

(12) EUROPEAN PATENT APPLICATION

(43) Date of publication:
03.12.1997 Bulletin 1997/49

(21) Application number: **97112541.4**

(22) Date of filing: **29.11.1991**

(51) Int. Cl.[6]: **B01L 7/00**, B01L 3/00, B01L 9/06, C12Q 1/68, G05D 23/19

(84) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI LU NL SE

(30) Priority: **29.11.1990 US 620606**
14.03.1991 US 670545

(62) Document number(s) of the earlier application(s) in accordance with Art. 76 EPC:
91311090.4 / 0 488 769

(71) Applicant:
The Perkin-Elmer Corporation
Emeryville, California 94608 (US)

(72) Inventors:
- **Mossa, Albert Carmelo**
  Trumbull, Connecticut 06611 (US)
- **Goven, Lisa May**
  Bridgeport, Connecticut 06606 (US)
- **Atwood, John Girdner**
  West Redding, Connecticut 06896 (US)
- **Williams,Fenton**
  Brookfield, Connecticut 06804 (US)
- **Woudenberg, Timothy M.**
  Bethel, Connecticut 06801 (US)
- **Margulies, Marcel**
  Scarsdale, New York 10583 (US)
- **Ragusa, Robert P.**
  Newton, Connecticut 06470 (US)
- **Leath, Richard**
  Berkeley, California 94707 (US)

(74) Representative:
Bizley, Richard Edward et al
Hepworth, Lawrence, Bryer & Bizley
Merlin House
Falconry Court
Baker's Lane
Epping Essex CM16 5DQ (GB)

Remarks:
This application was filed on 22 - 07 - 1997 as a divisional application to the application mentioned under INID code 62.

(54) Apparatus and containers for performing polymerase chain reaction

(57) A thermocycler apparatus for performing polymerase chain reaction (PCR) comprises a heating block (12) and heated cover (14) in which sample tubes (324,326) are retained, heated and cooled as required. The heating of the upper portions and caps of sample tubes (324,326) in use prevents condensation inside the tube caps thereby eliminating the need for a layer of oil floating on the surface of the sample liquid.

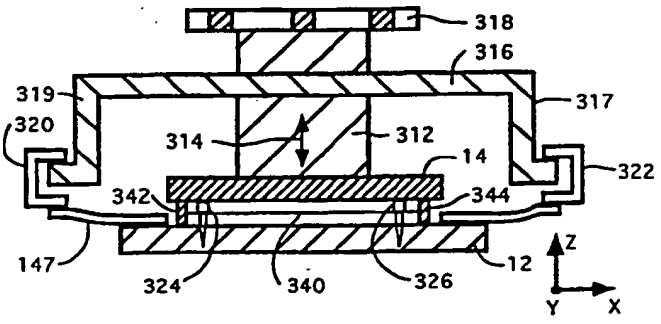


FIG. 19

EP 0 810 030 A1

European Patent Office

EUROPEAN SEARCH REPORT

Application Number
EP 97 11 2541

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
Y	EP 0 388 159 A (SEIKO INSTR INC) 19 September 1990 * column 1, line 6 - line 36; figures 2,4 * ---	1,5	B01L7/00 B01L3/00 B01L9/06 C12Q1/68 G05D23/19
Y	DE 26 03 683 A (LOO HANS MICHAEL VAN DE DR RER) 11 August 1977 * page 2, line 1 - line 17 * * page 2, line 26 - page 3, line 33; figures * ---	1,5	
A	EP 0 311 440 A (SEIKO INSTR INC) 12 April 1989 * the whole document * ---	1,5	
A	US 3 483 997 A (RITTER HARRY W) 16 December 1969 * the whole document * ---	1,5,9	
X	DE 88 08 738 U (DIEKMANN) 1 September 1988 * page 3, line 4 - line 26 * * page 5, line 8 - line 20; figure * -----	6-11	

TECHNICAL FIELDS SEARCHED (Int.Cl.6)

B01L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	11 September 1997	Hocquet, A

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

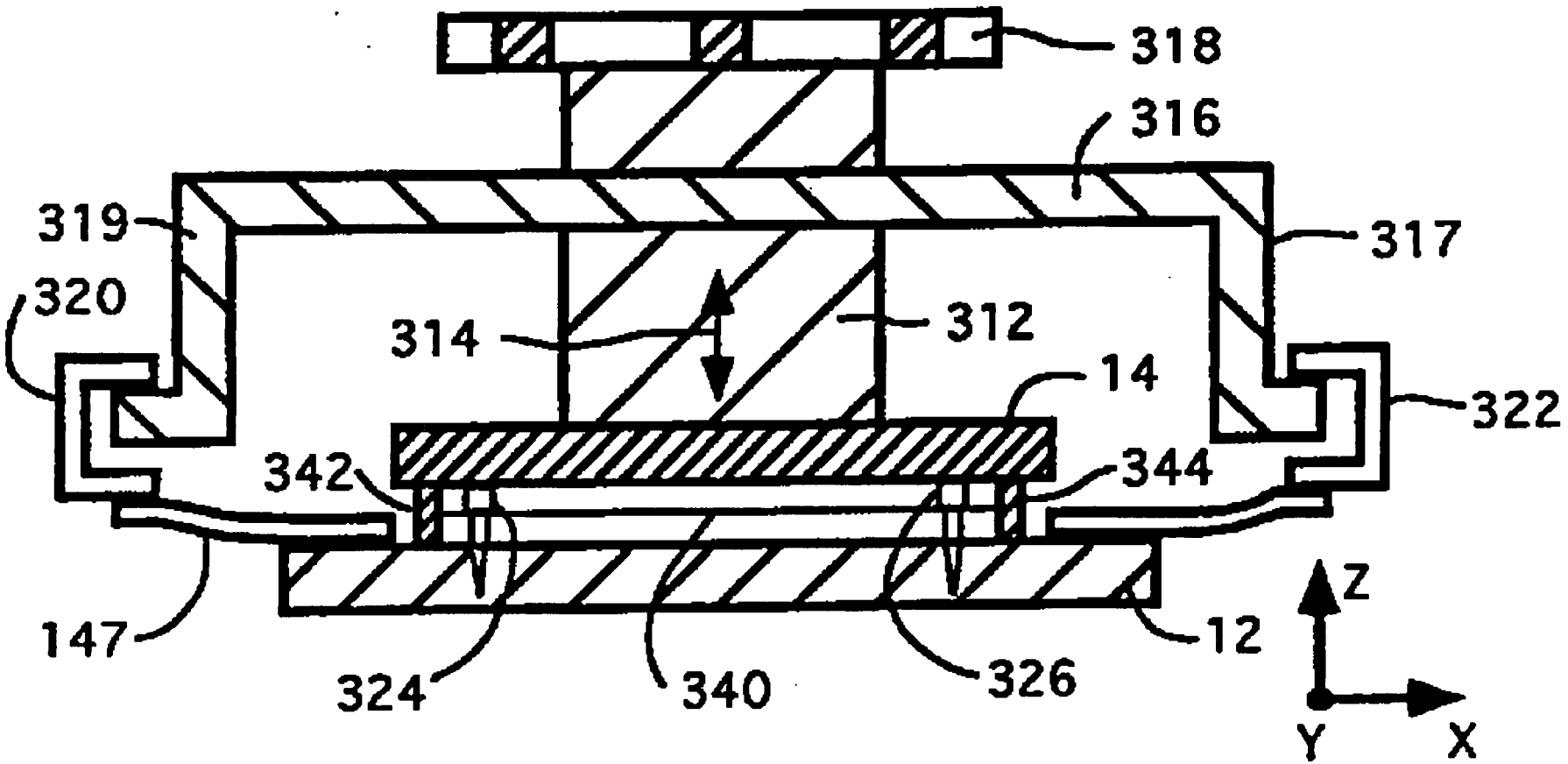


FIG. 19

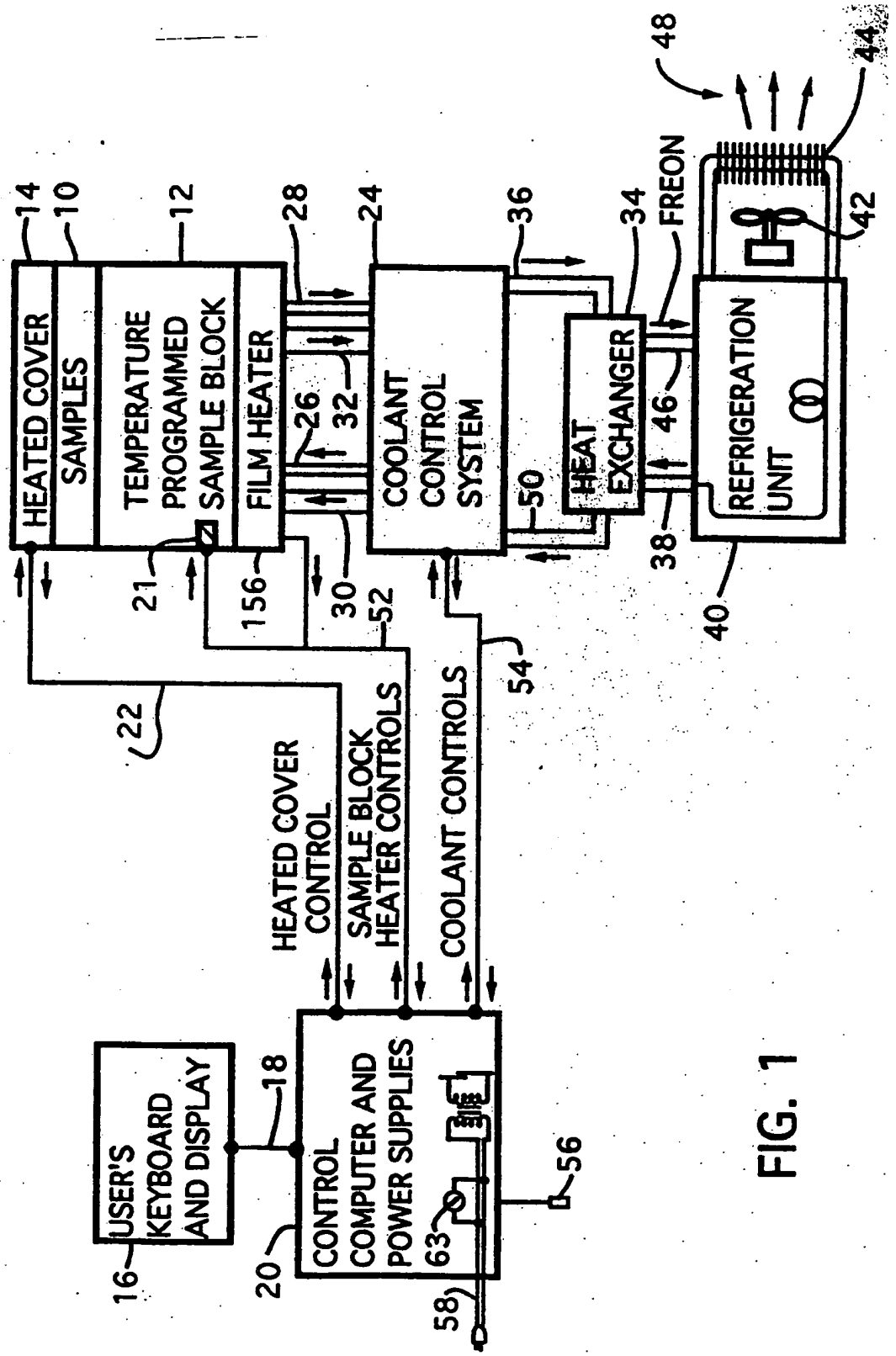

HEATED COVER
SAMPLES
TEMPERATURE PROGRAMMED SAMPLE BLOCK
FILM HEATER
COOLANT CONTROL SYSTEM
HEAT EXCHANGER
FREON
REFRIGERATION UNIT
HEATED COVER CONTROL
SAMPLE BLOCK HEATER CONTROLS
COOLANT CONTROLS
USER'S KEYBOARD AND DISPLAY
CONTROL COMPUTER AND POWER SUPPLIES
10
12
14
16
18
20
21
22
24
26
28
30
32
34
36
38
40
42
44
46
48
50
52
54
56
58
63
156

FIG. 1

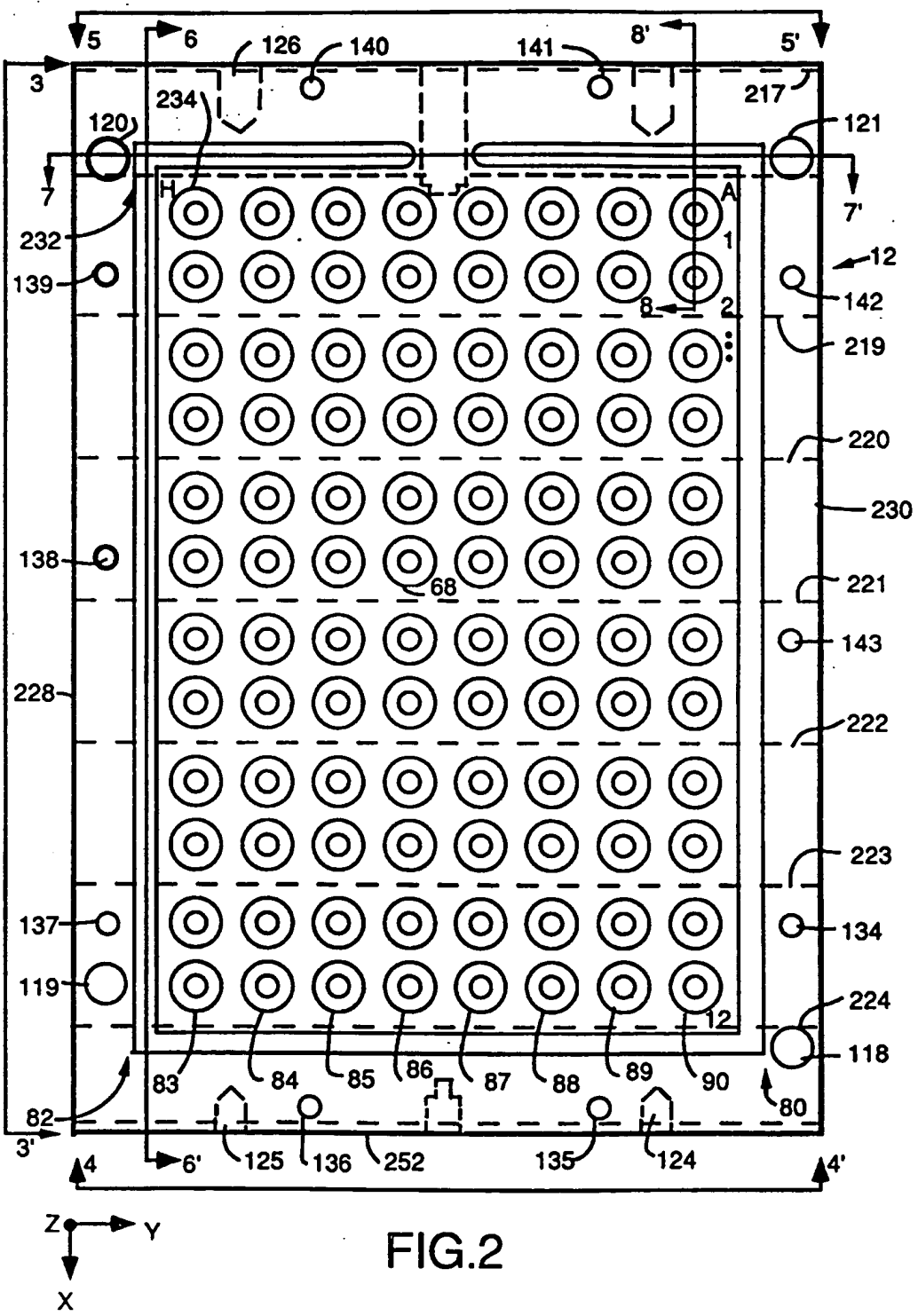

5
6
126
140
141
8'
5'
3
234
217
120
121
7
7'
H
A
232
1
12
139
8
2
142
219
220
230
138
68
221
143
228
222
223
137
134
119
224
12
118
83
84
85
86
87
88
89
90
80
82
3'
4
6'
125
136
252
135
124
4'
Z
Y
X

FIG.2

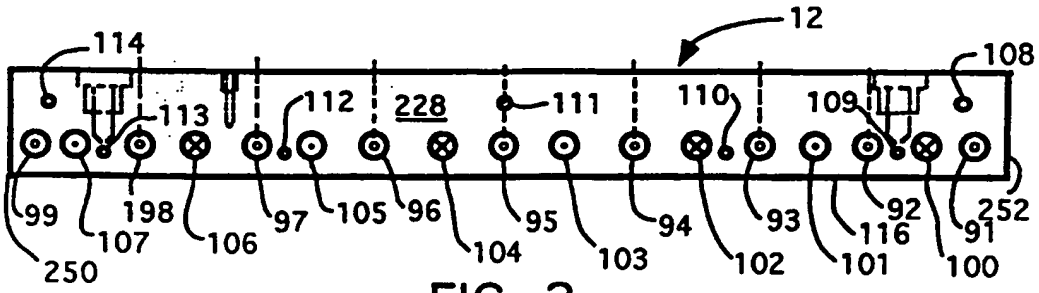


FIG. 3

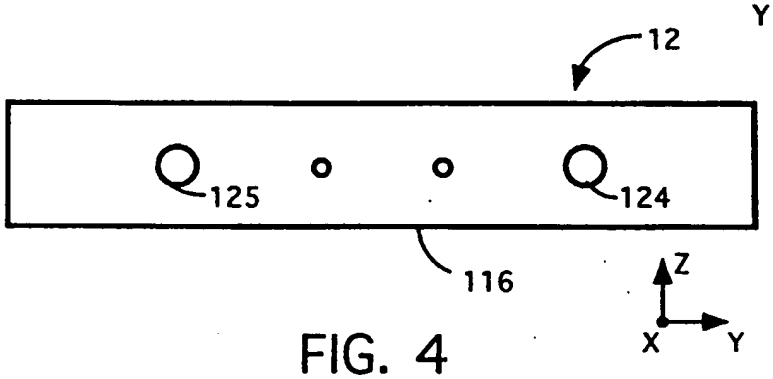


FIG. 4

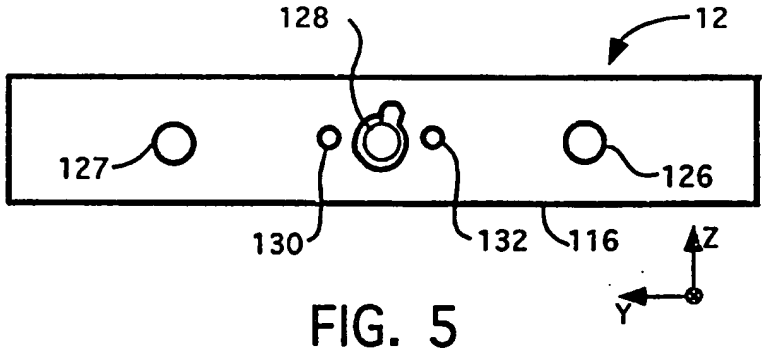


FIG. 5

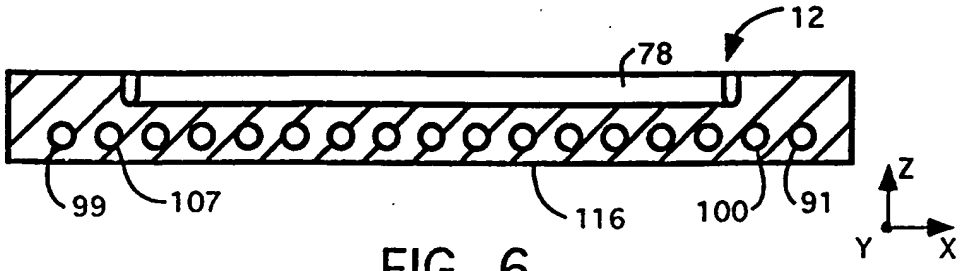


FIG. 6

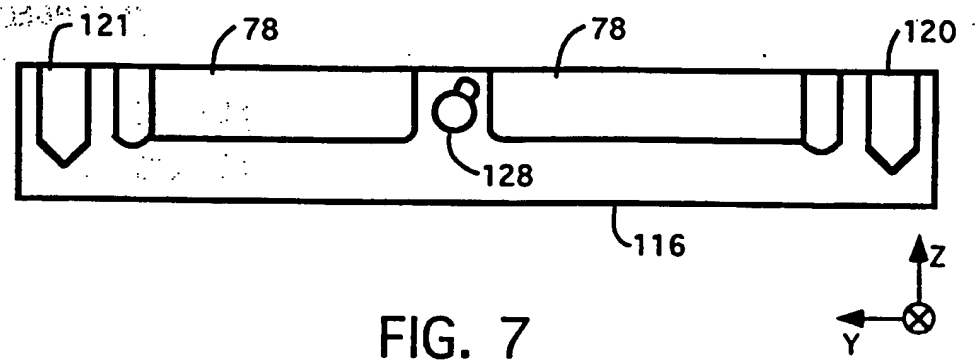


FIG. 7

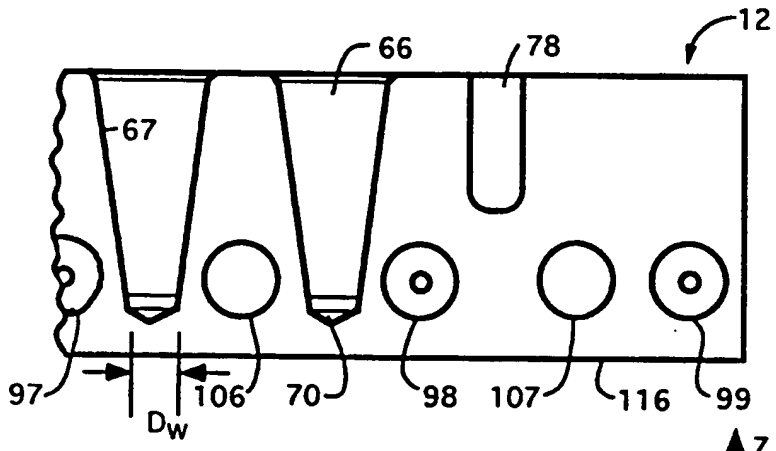


FIG. 8

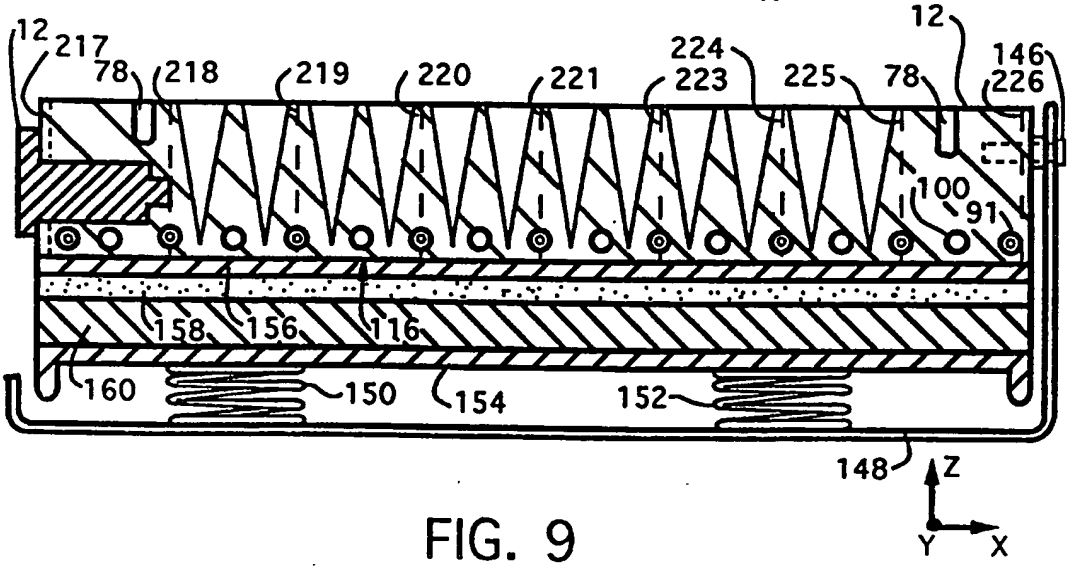


FIG. 9

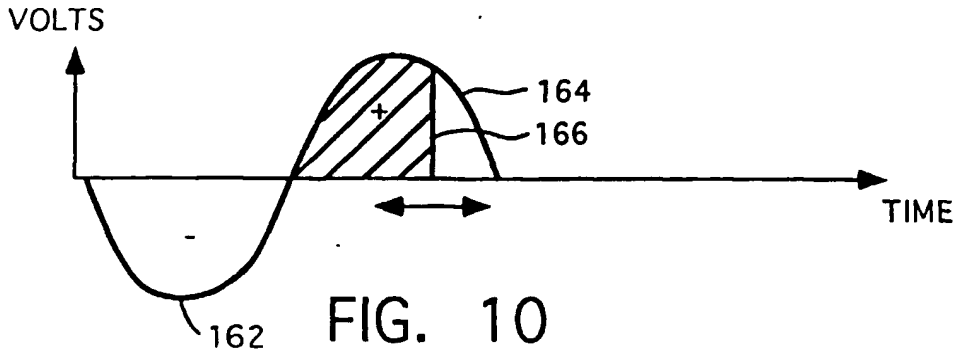


FIG. 10

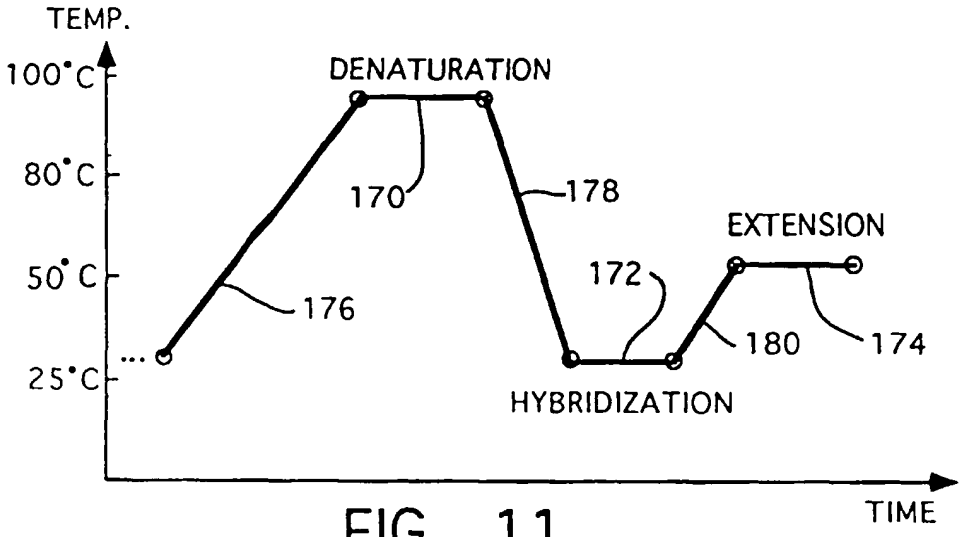


FIG. 11

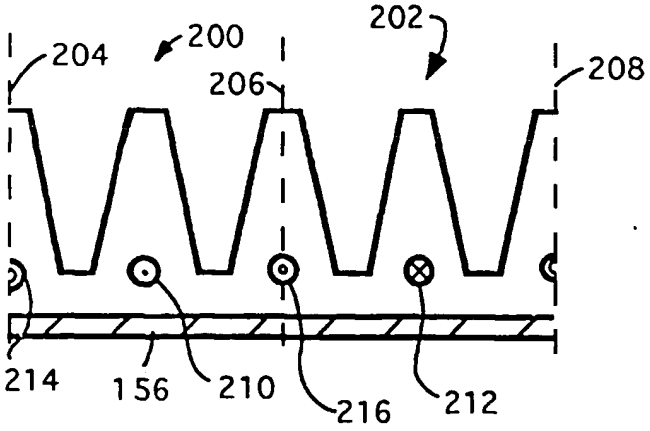


FIG. 12

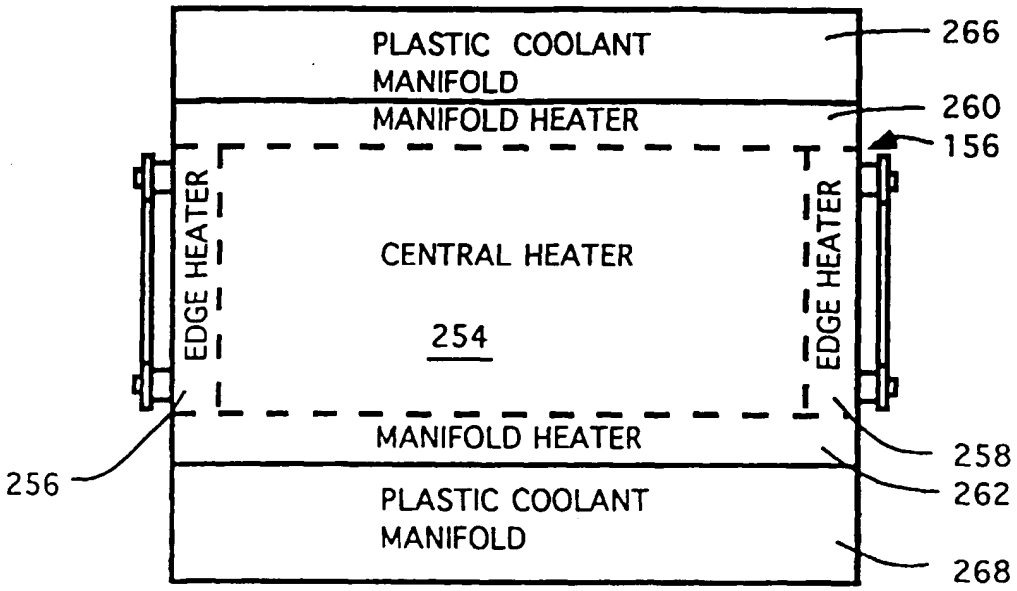

PLASTIC COOLANT MANIFOLD
MANIFOLD HEATER
EDGE HEATER
CENTRAL HEATER
254
EDGE HEATER
MANIFOLD HEATER
PLASTIC COOLANT MANIFOLD
266
260
156
256
258
262
268

FIG. 13

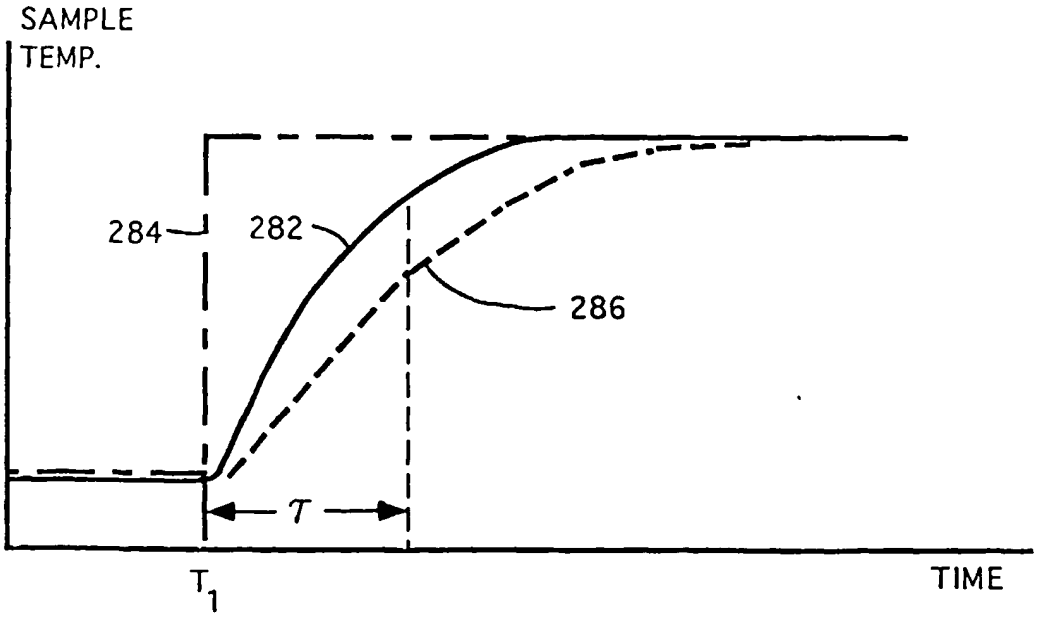

SAMPLE TEMP.
284
282
286
T
T1
TIME

FIG. 14

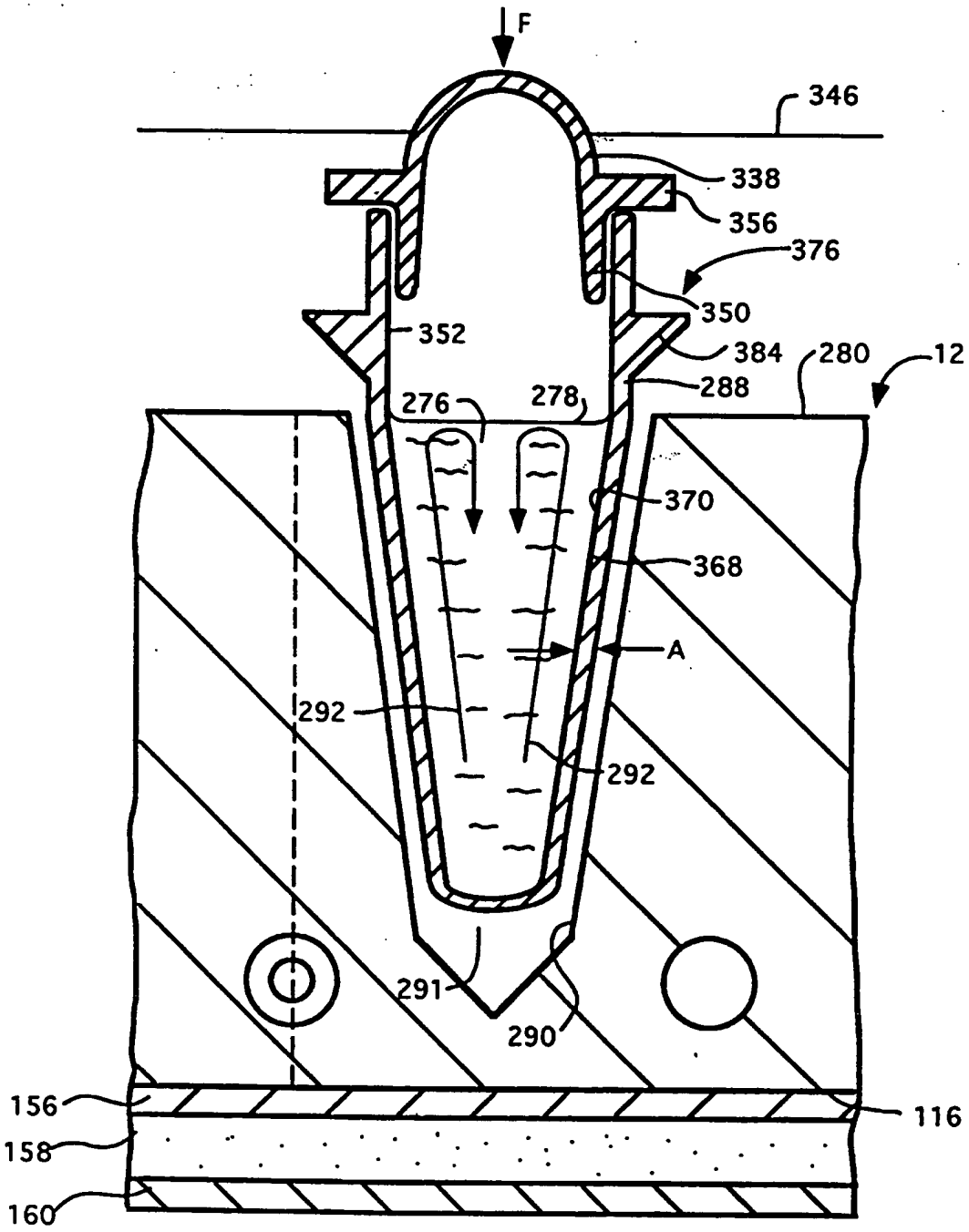

F
346
338
356
376
350
352
384
280
12
288
276
278
370
368
A
292
292
291
290
156
158
160
116

FIG. 15

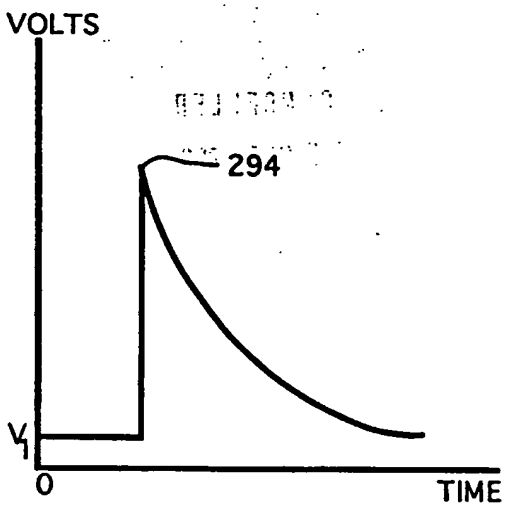


FIG. 16A

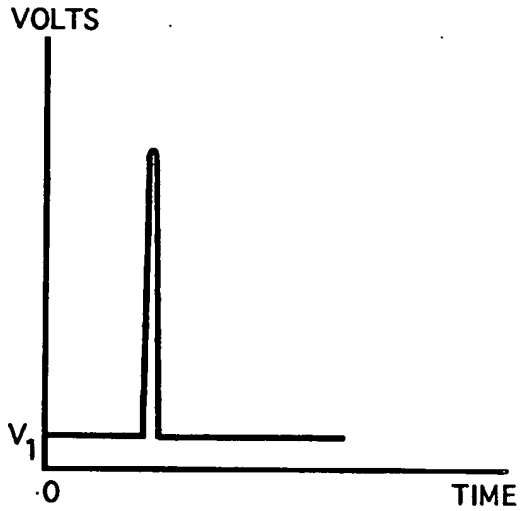


FIG. 16B

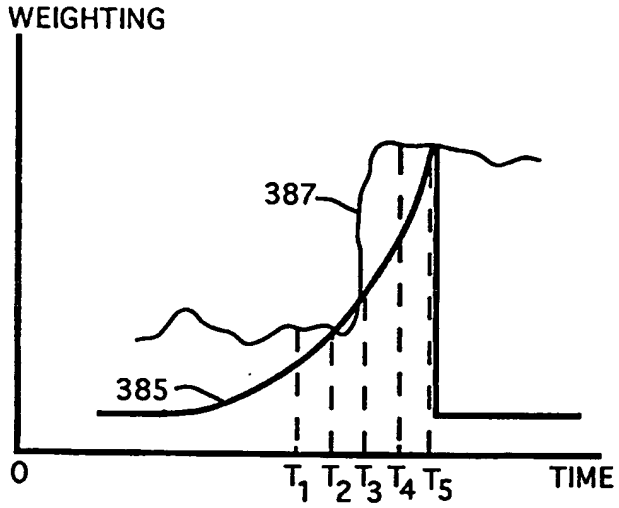


FIG. 16C

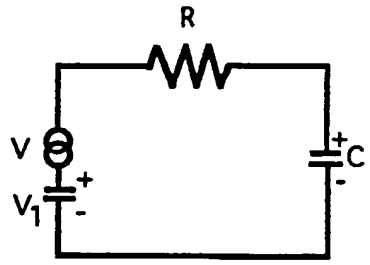


FIG. 16D

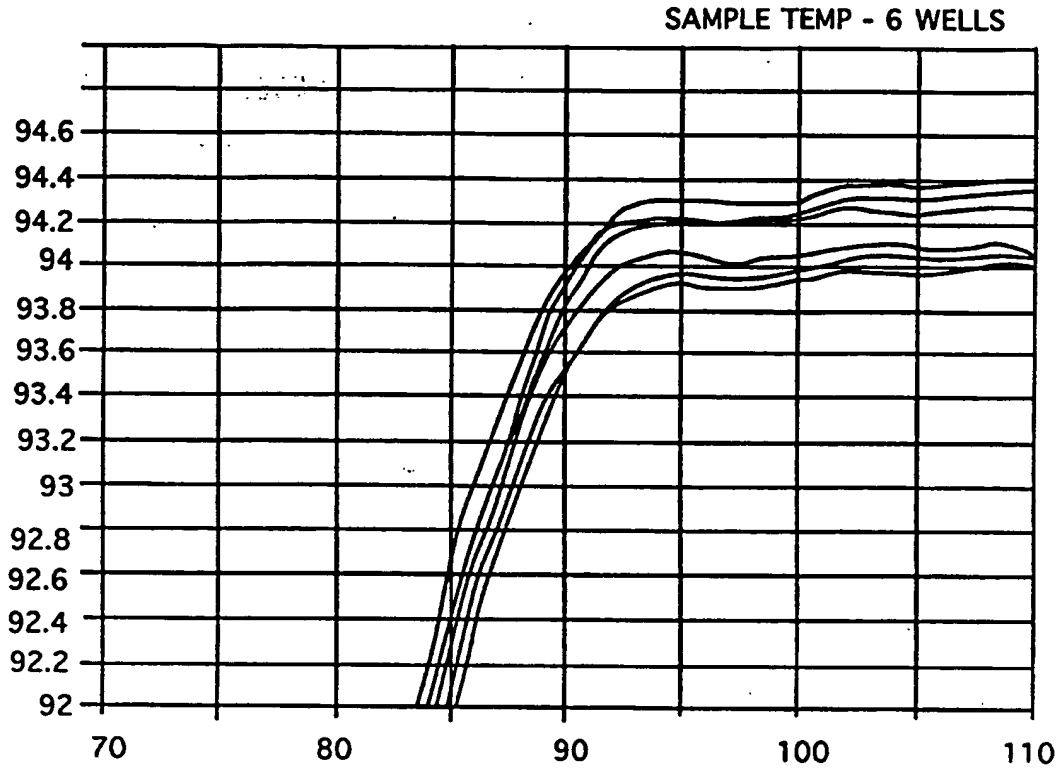

SAMPLE TEMP - 6 WELLS
94.6
94.4
94.2
94
93.8
93.6
93.4
93.2
93
92.8
92.6
92.4
92.2
92
70
80
90
100
110

FIG. 17

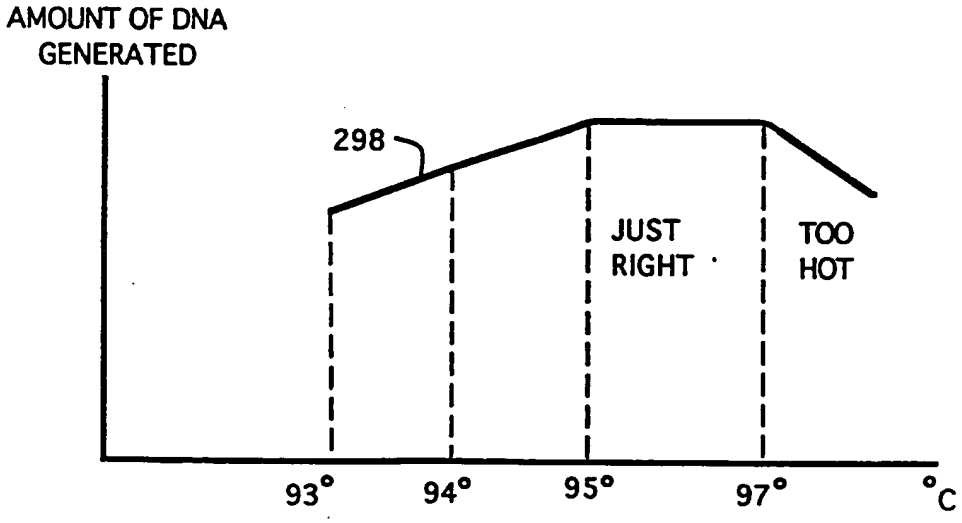

AMOUNT OF DNA GENERATED
298
JUST RIGHT
TOO HOT
93°
94°
95°
97°
°C

FIG. 18

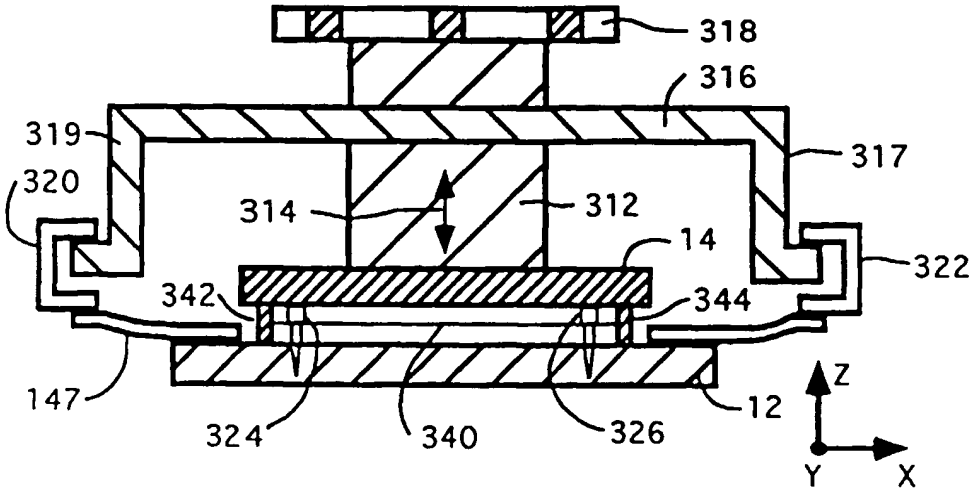

318
316
319
317
320
314
312
14
322
342
344
147
324
340
326
12
Z
Y
X

FIG. 19

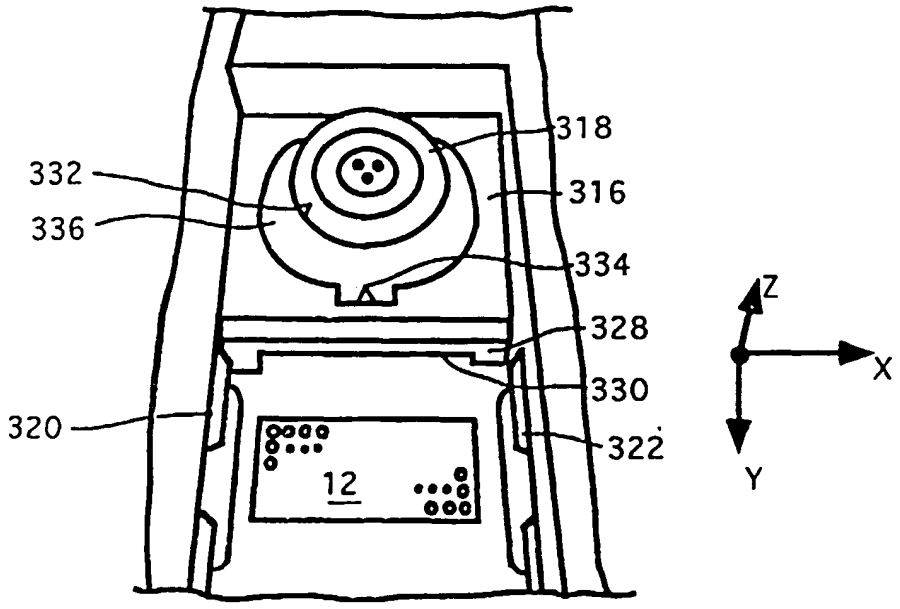

318
332
316
336
334
328
330
320
322
12
Z
X
Y

FIG. 20

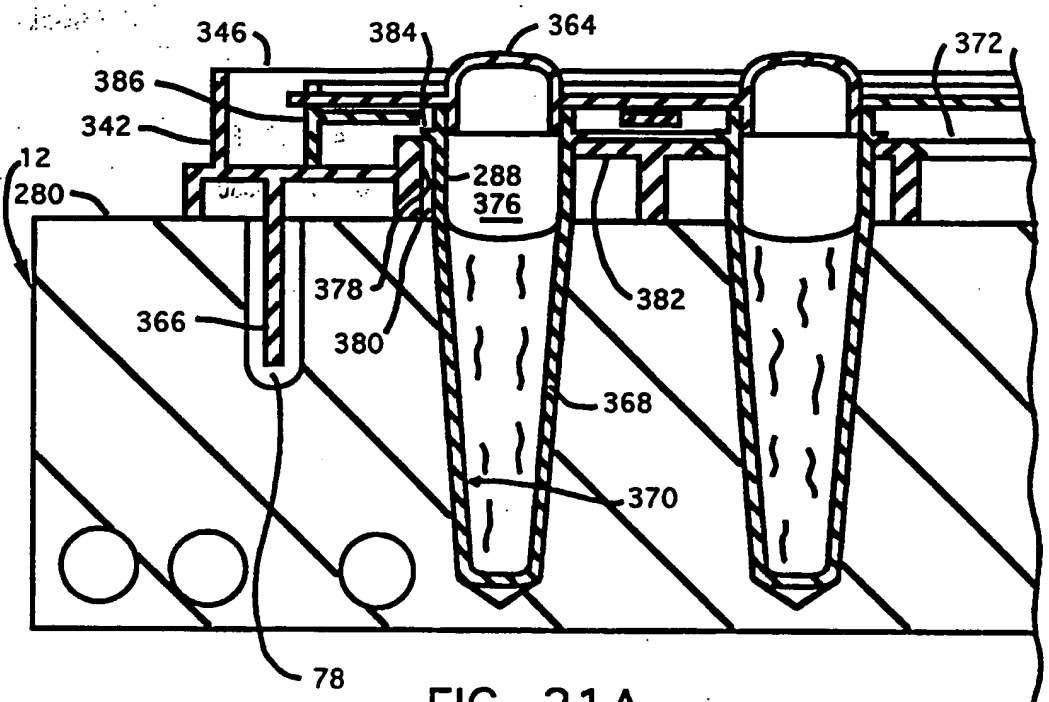


FIG 21A

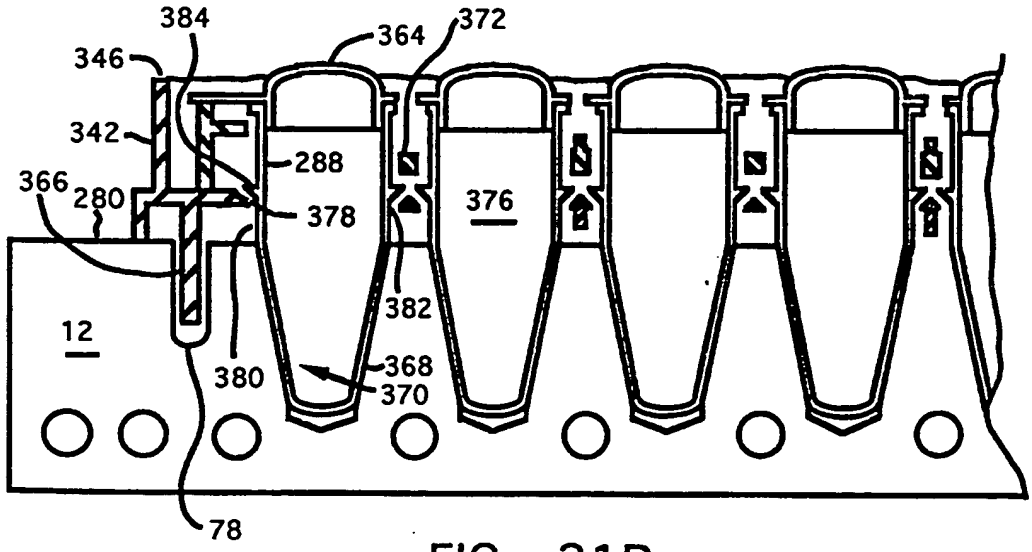


FIG. 21B

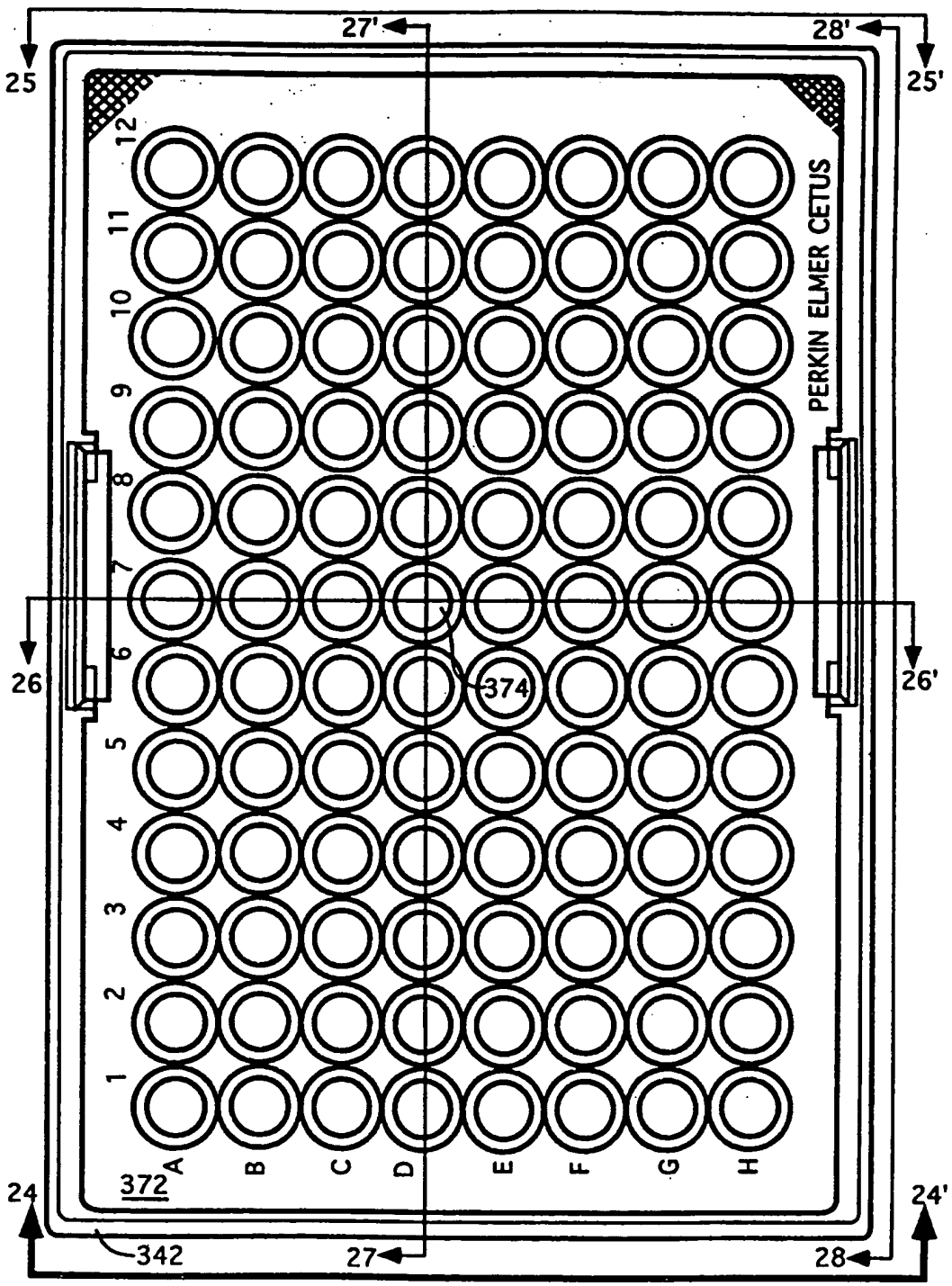

27'
28'
25
25'
12
11
10
9
8
7
6
5
4
3
2
1
PERKIN ELMER CETUS
26
26'
374
A
B
C
D
E
F
G
H
372
24
24'
342
27
28

FIG. 22

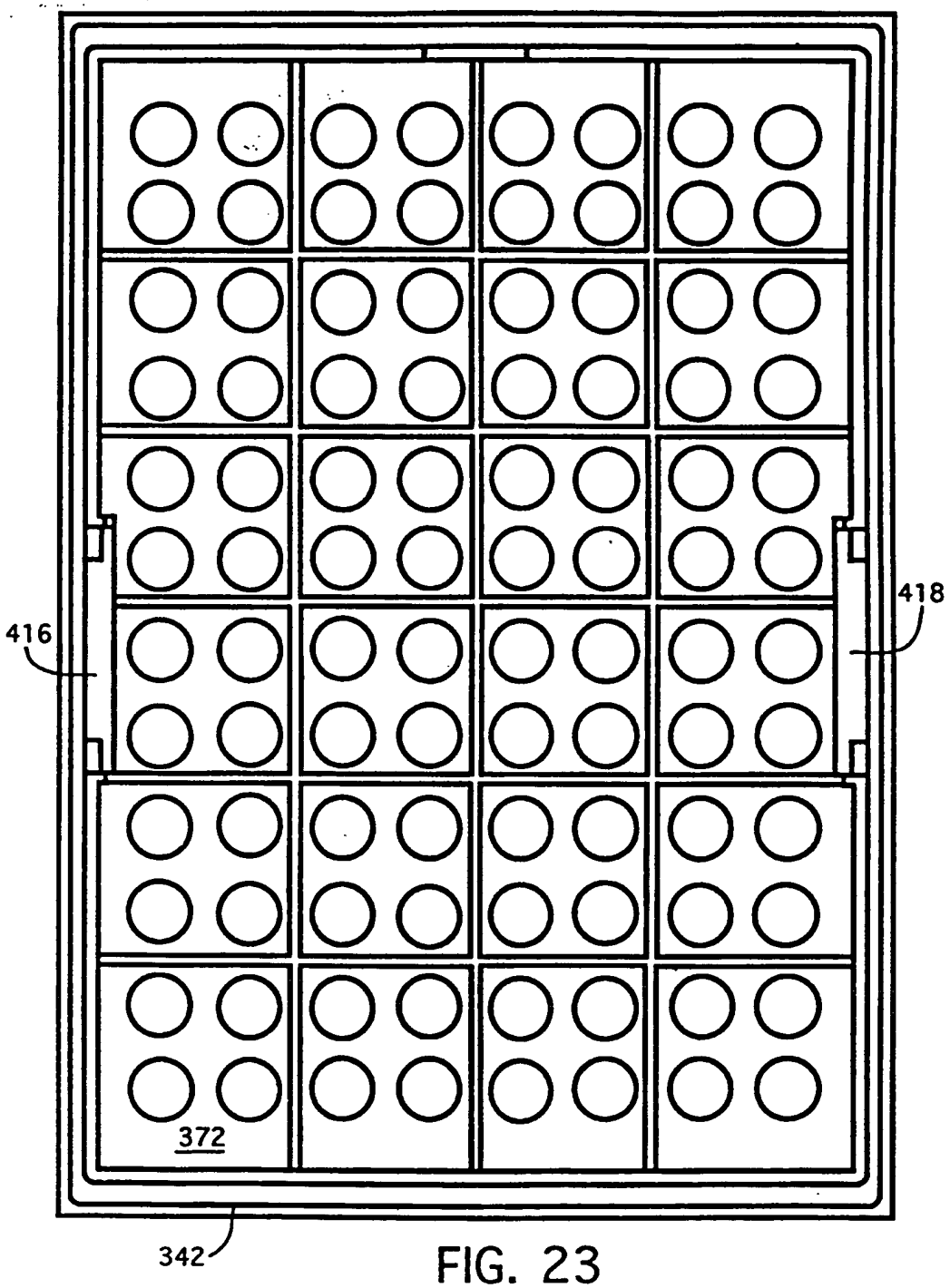


FIG. 23

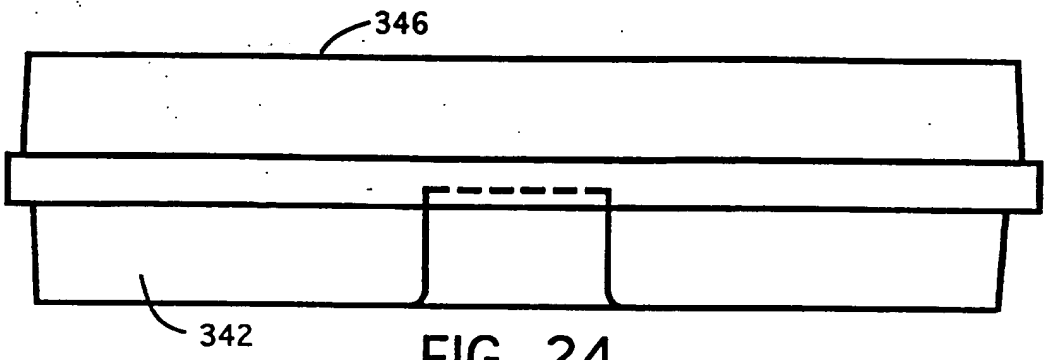


FIG. 24

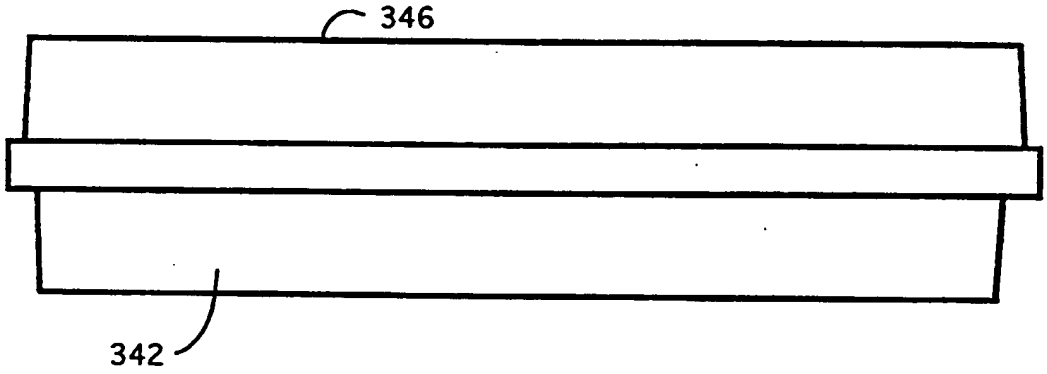


FIG. 25

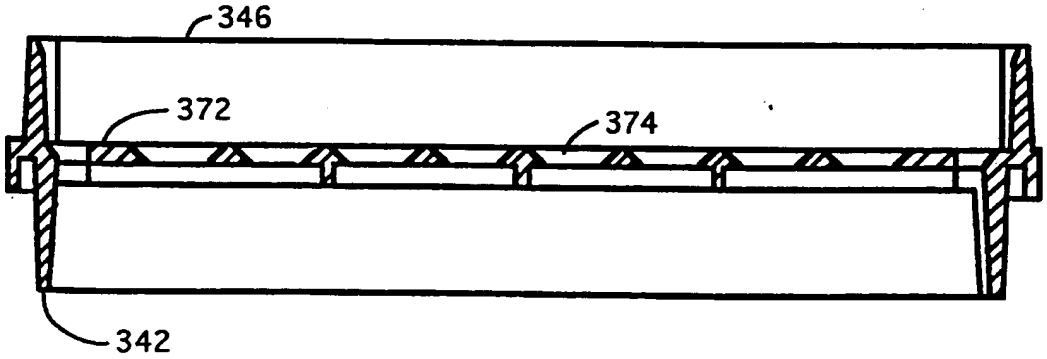


FIG. 26

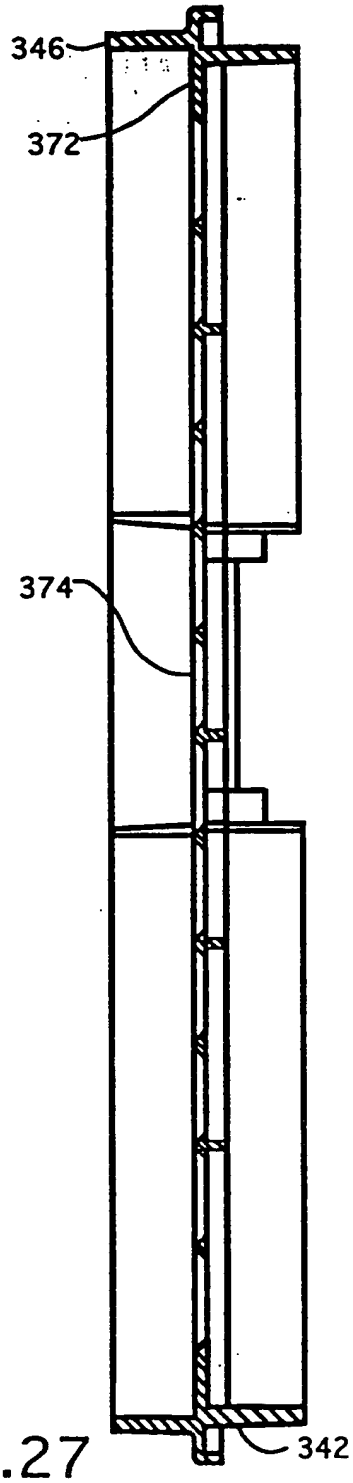


FIG.27

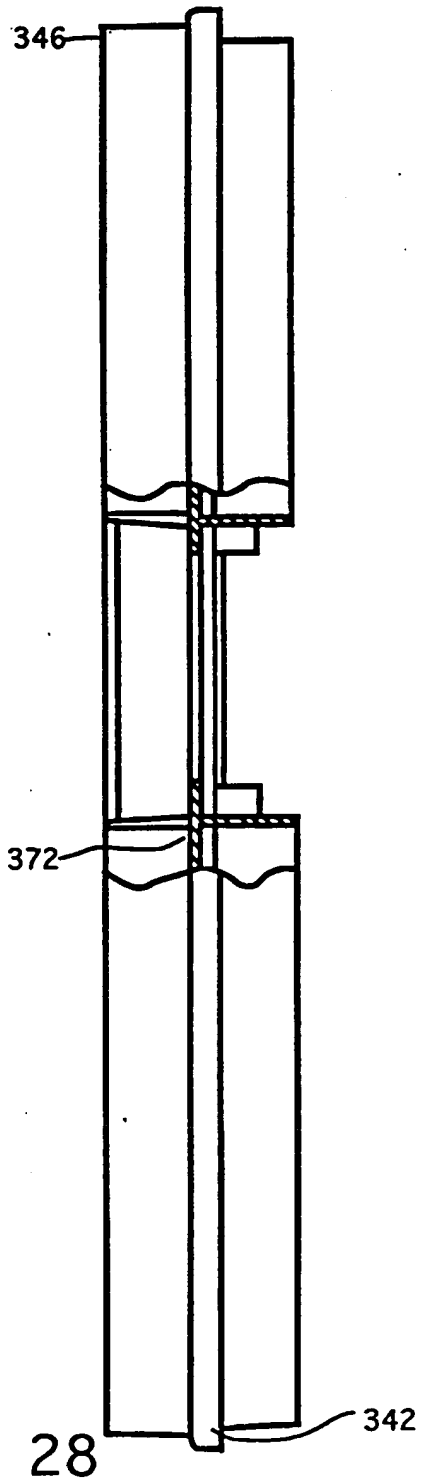


FIG. 28

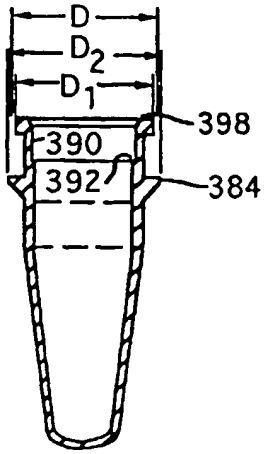


FIG 29

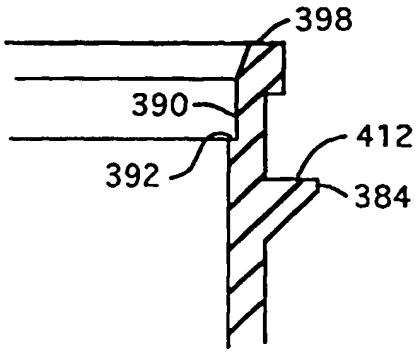


FIG 30

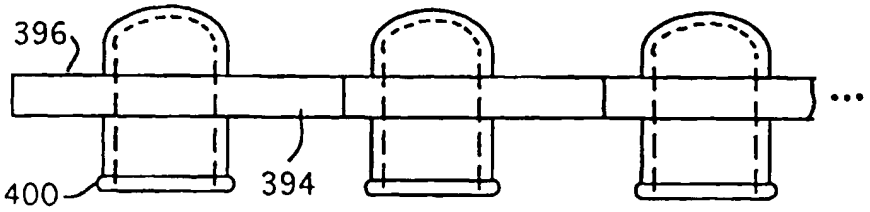


FIG 31

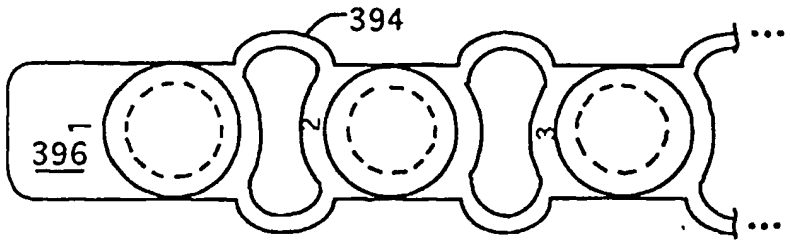


FIG 32

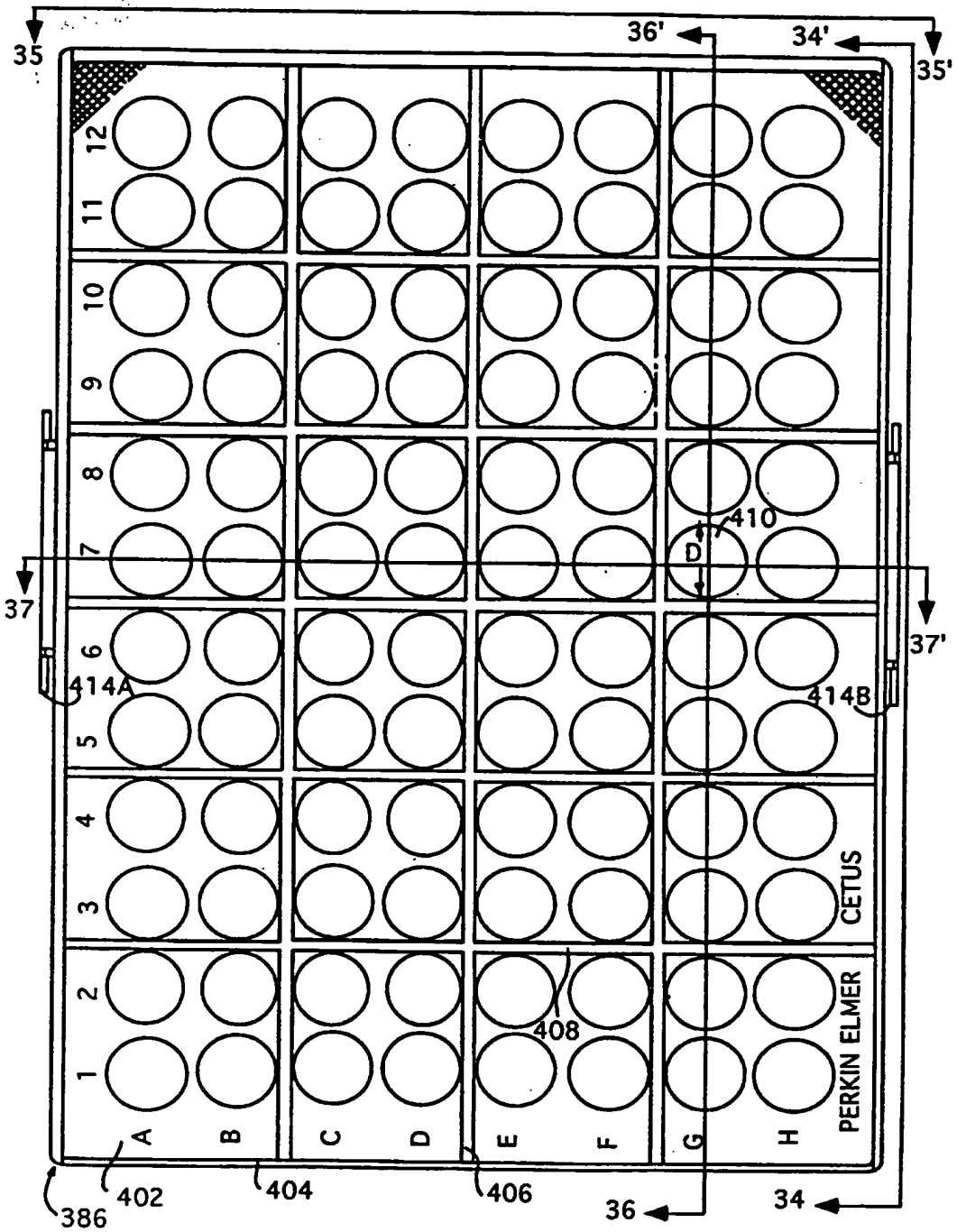

35
36'
34'
35'
12
11
10
9
8
7
6
5
4
3
2
1
A
B
C
D
E
F
G
H
410
D
37
37'
414A
414B
CETUS
PERKIN ELMER
408
386
402
404
406
36
34

FIG. 33

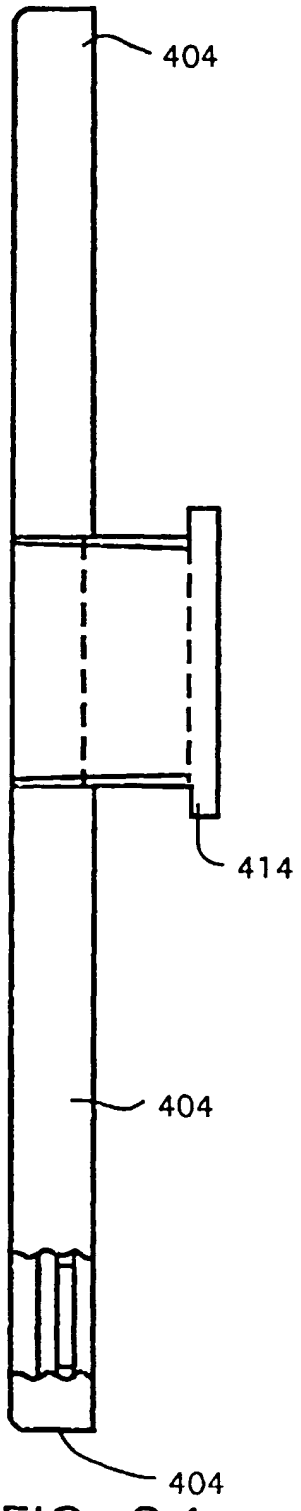


FIG. 34

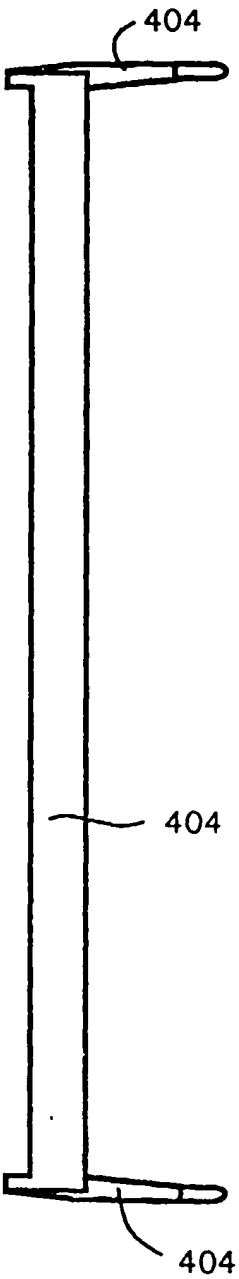


FIG.35

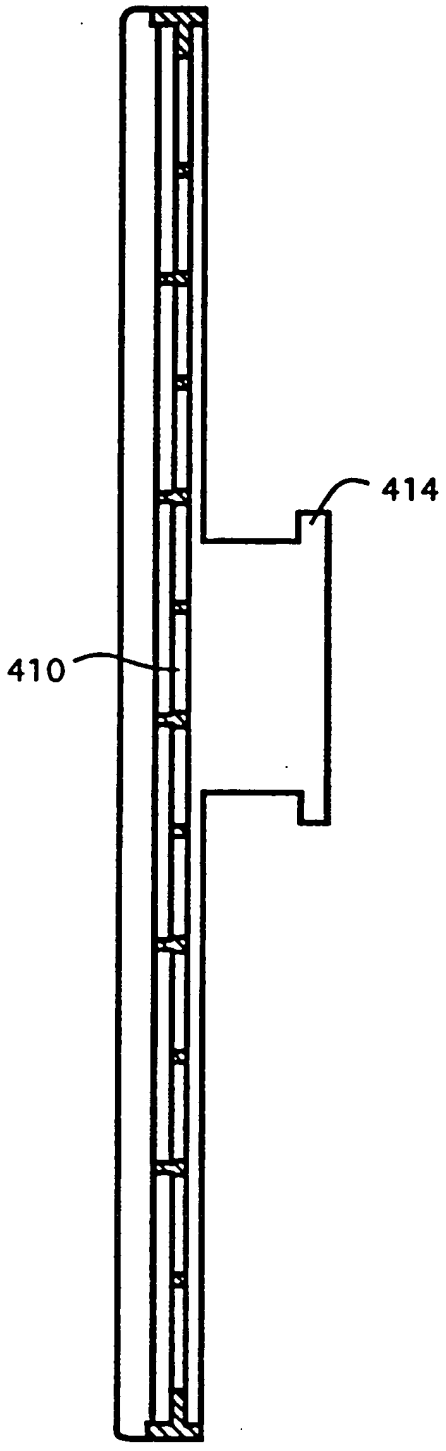


FIG. 36

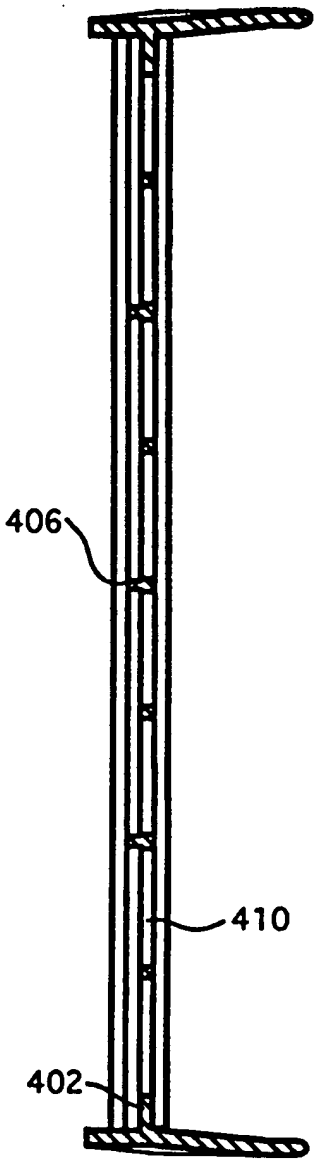


FIG. 37

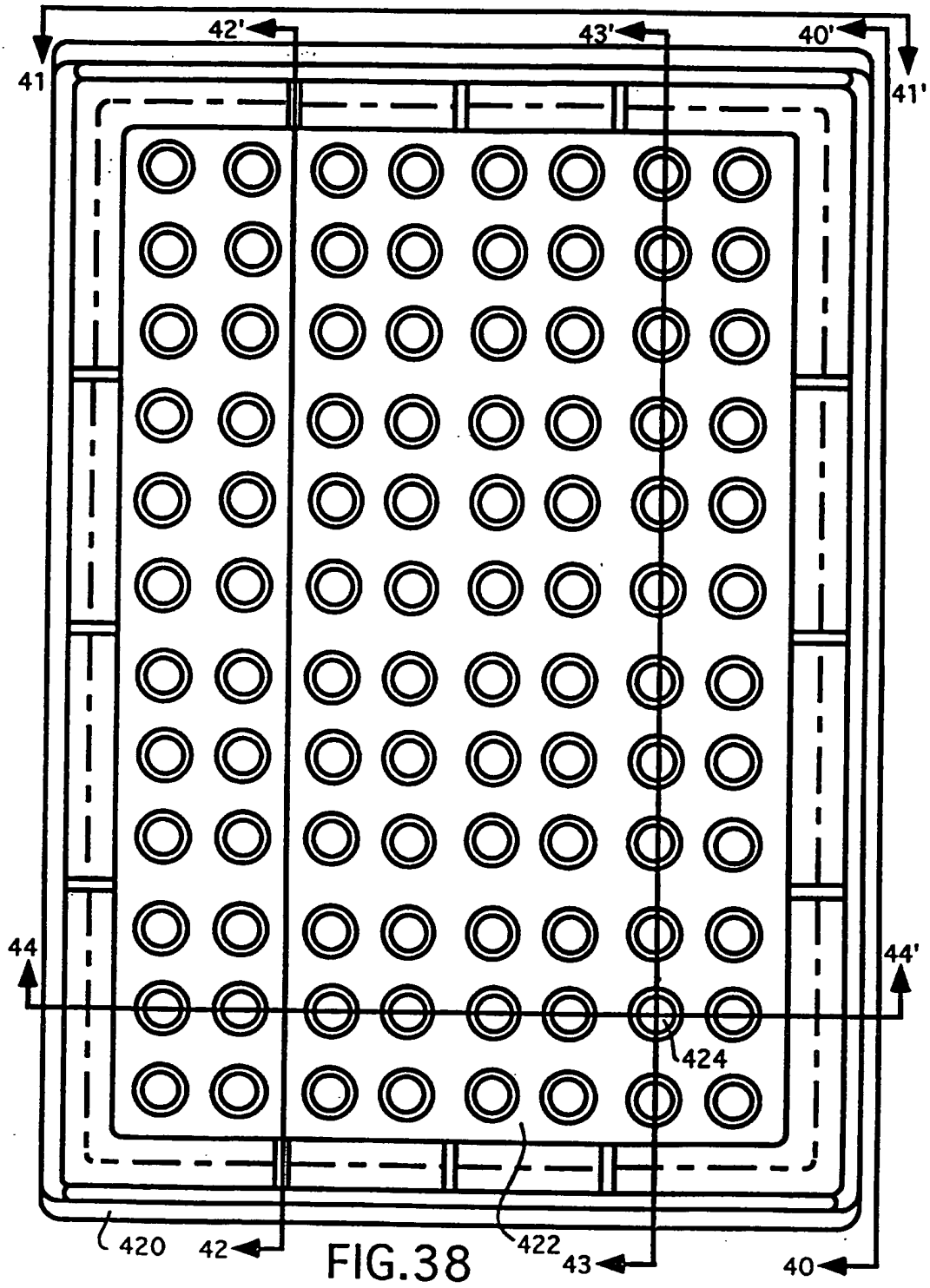


FIG.38

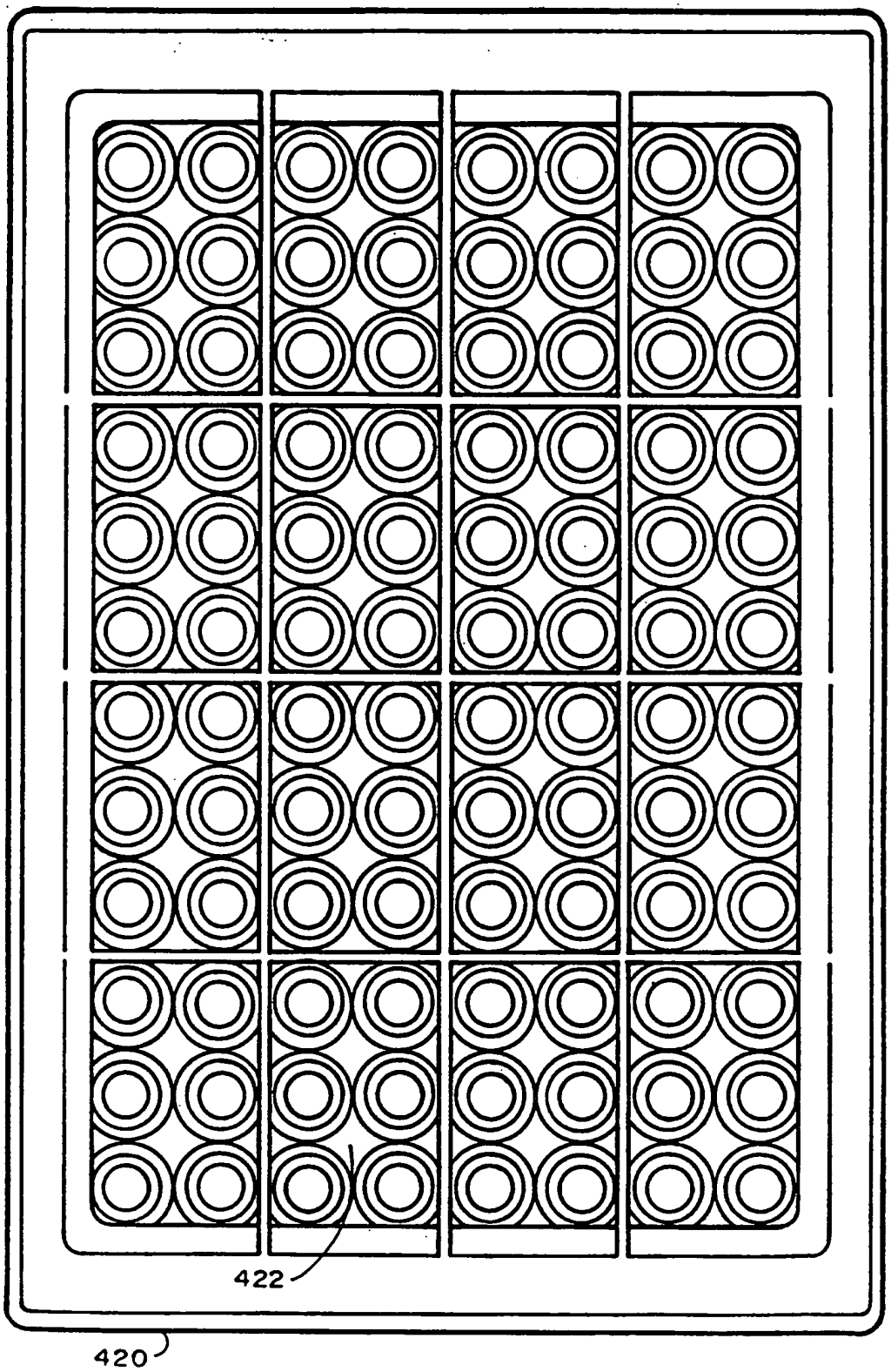


FIG. 39

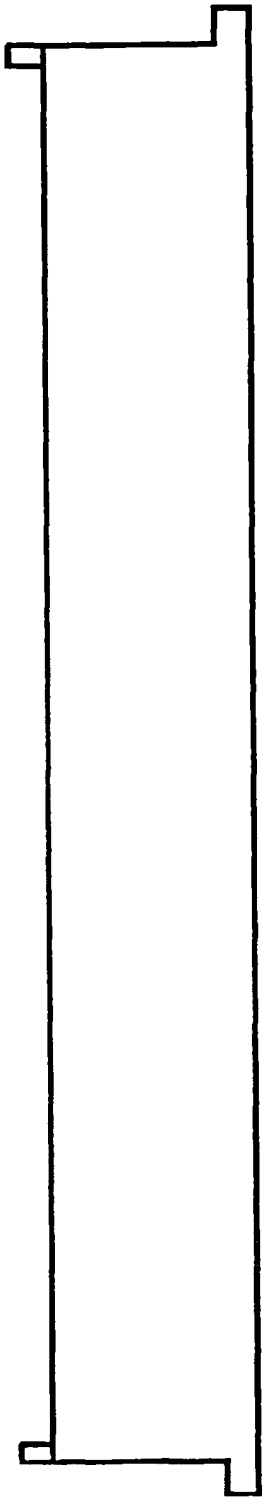


FIG. 40

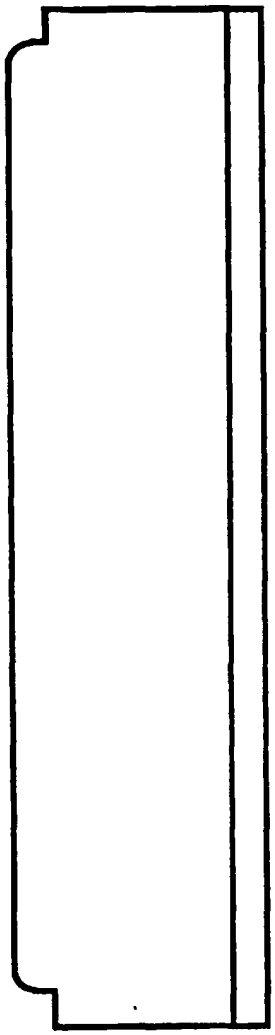


FIG. 41

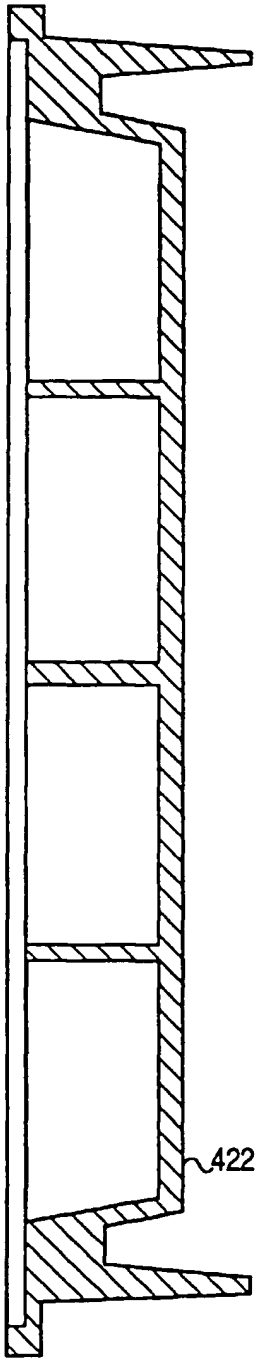


FIG. 42

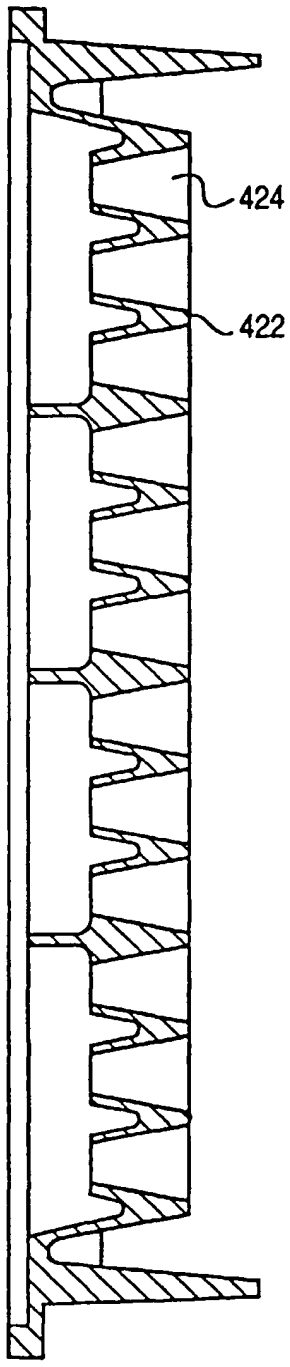


FIG. 43

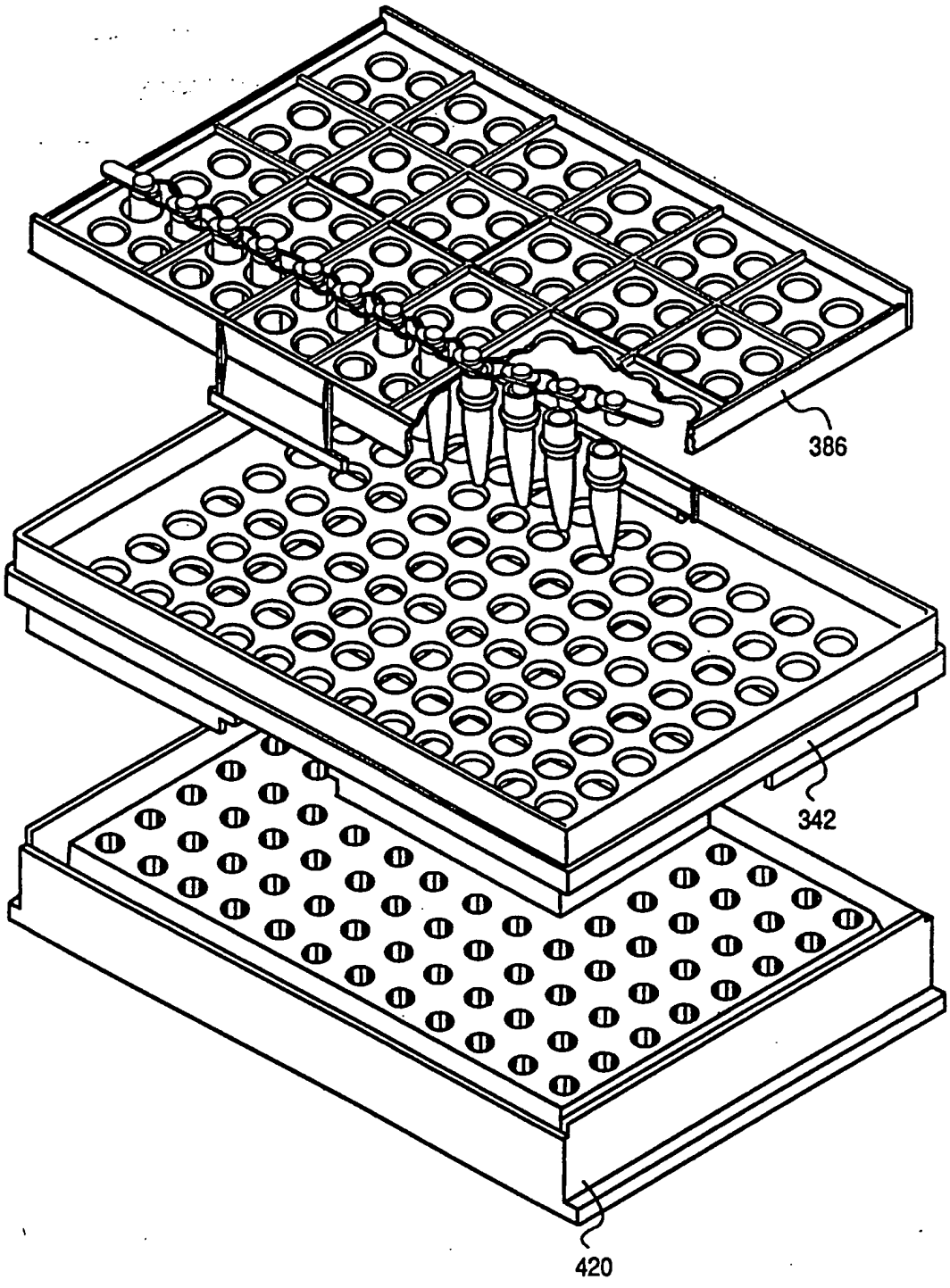


FIG. 45

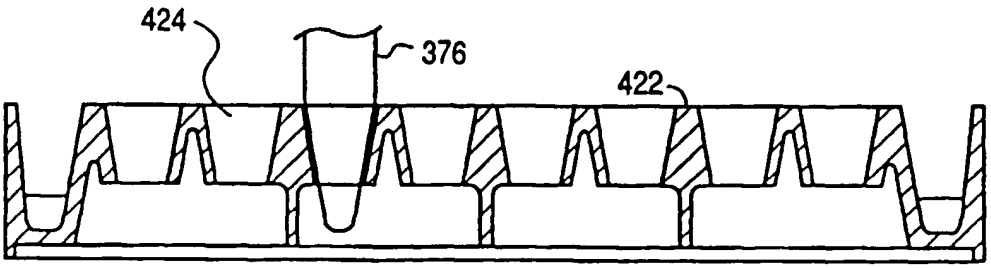


FIG. 44

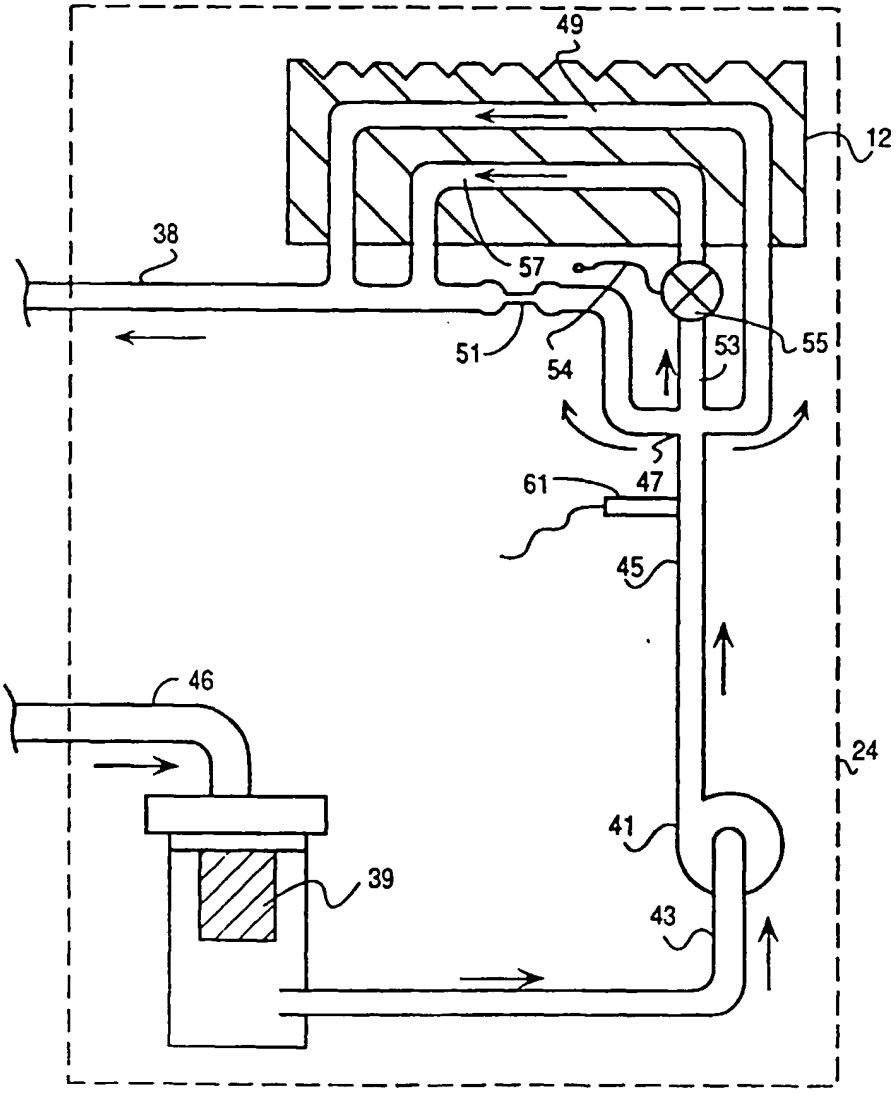
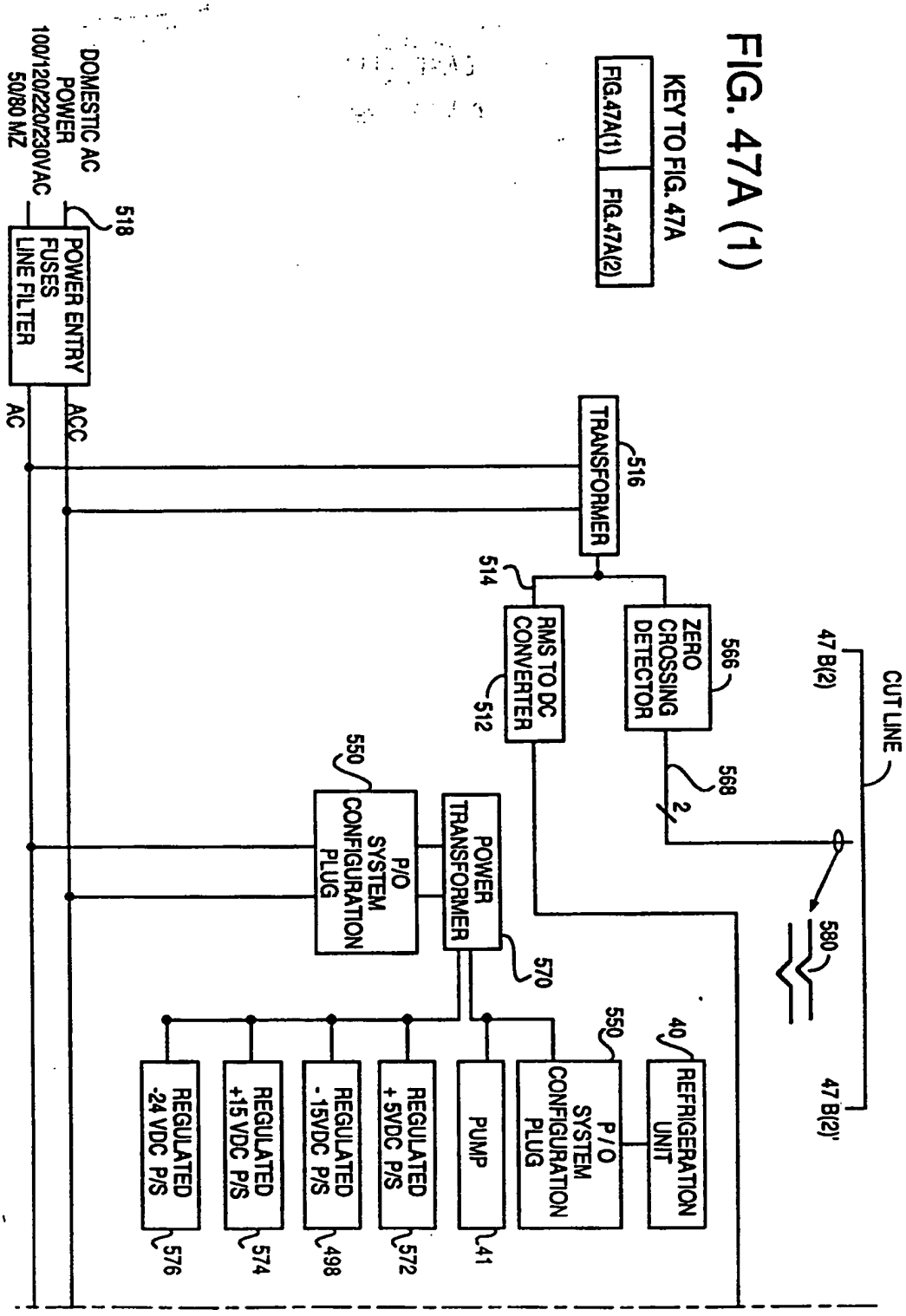


FIG. 46

FIG. 47A (1)


KEY TO FIG. 47A
FIG.47A(1)
FIG.47A(2)
DOMESTIC AC POWER
100/120/220/230VAC
50/80 MZ
518
POWER ENTRY
FUSES
LINE FILTER
AC
ACC
516
TRANSFORMER
514
RMS TO DC CONVERTER
512
ZERO CROSSING DETECTOR
566
568
47 B(2)
CUT LINE
580
47 B(2)'
550
P/O SYSTEM CONFIGURATION PLUG
POWER TRANSFORMER
570
40
REFRIGERATION UNIT
PUMP
41
REGULATED +5VDC P/S
572
REGULATED -15VDC P/S
498
REGULATED +15 VDC P/S
574
REGULATED -24 VDC P/S
576

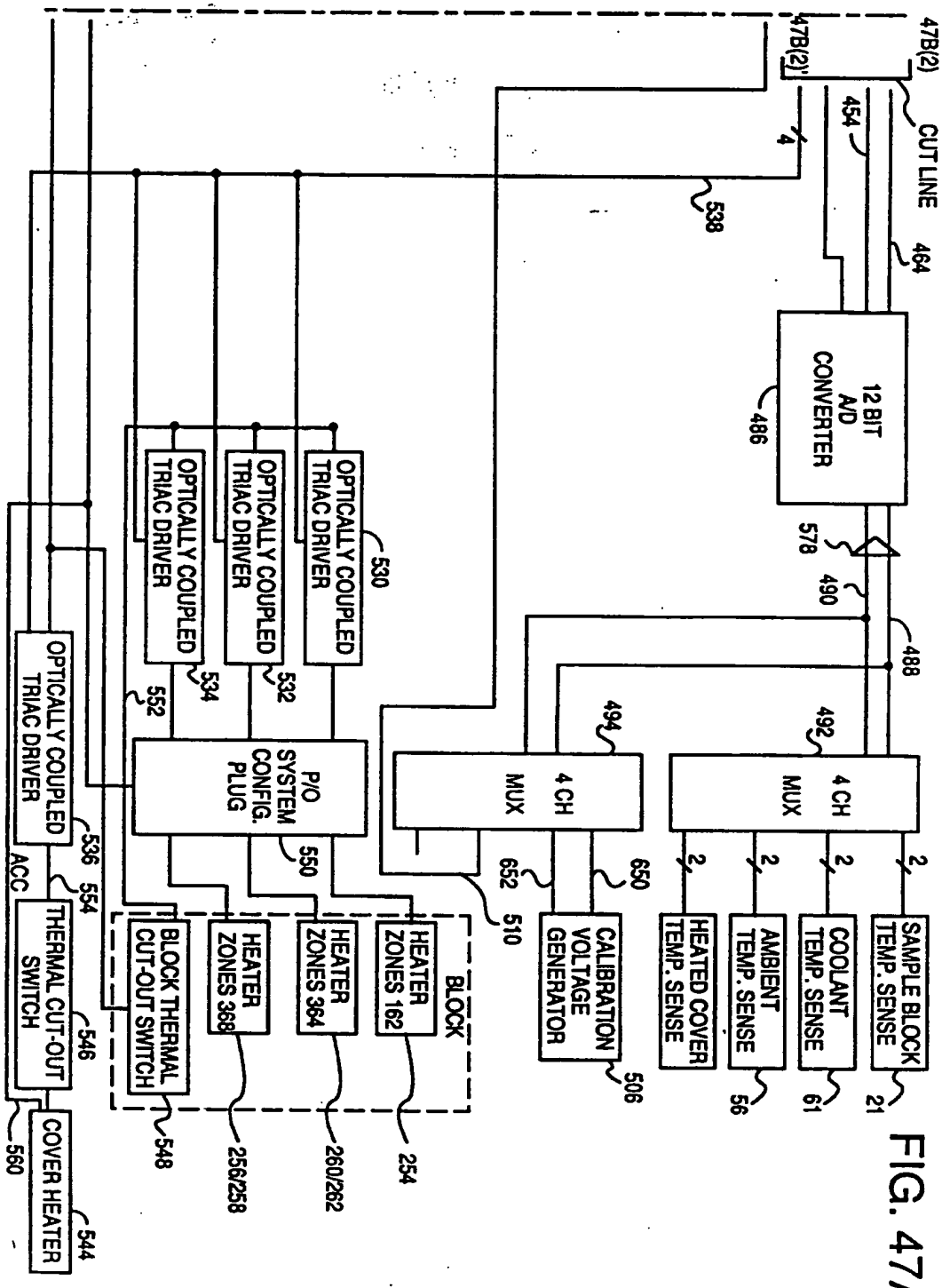

47B(2)
47B(2)'
CUT LINE
454
464
4
538
12 BIT A/D CONVERTER
486
578
490
488
494
492
4 CH MUX
4 CH MUX
2
2
2
2
650
652
510
506
SAMPLE BLOCK TEMP. SENSE
COOLANT TEMP. SENSE
AMBIENT TEMP. SENSE
HEATED COVER TEMP. SENSE
CALIBRATION VOLTAGE GENERATOR
21
61
56
OPTICALLY COUPLED TRIAC DRIVER
530
532
534
552
P/O SYSTEM CONFIG. PLUG
550
BLOCK
HEATER ZONES 162
HEATER ZONES 364
HEATER ZONES 368
BLOCK THERMAL CUT-OUT SWITCH
254
260/262
256/258
548
OPTICALLY COUPLED TRIAC DRIVER
536
554
ACC
THERMAL CUT-OUT SWITCH
546
560
COVER HEATER
544

FIG. 47A (2)

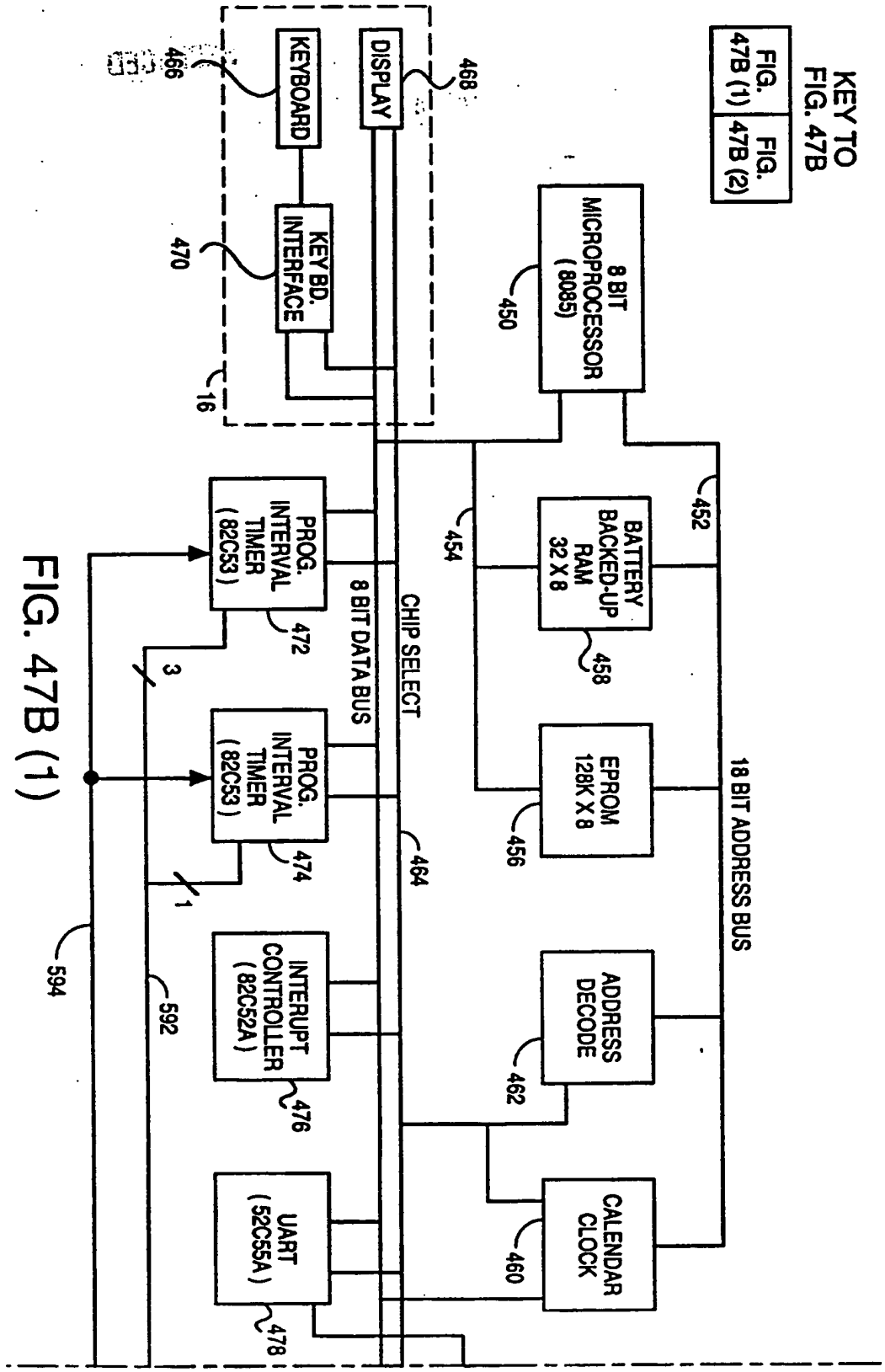

KEY TO FIG. 47B
FIG. 47B (1)
FIG. 47B (2)
8 BIT MICROPROCESSOR (8085)
450
BATTERY BACKED-UP RAM 32 X 8
458
EPROM 128K X 8
456
ADDRESS DECODE
462
CALENDAR CLOCK
460
18 BIT ADDRESS BUS
452
454
8 BIT DATA BUS
CHIP SELECT
464
PROG. INTERVAL TIMER (82C53)
472
PROG. INTERVAL TIMER (82C53)
474
INTERUPT CONTROLLER (82C52A)
476
UART (52C55A)
478
3
1
592
594
DISPLAY
468
KEYBOARD
466
KEY BD. INTERFACE
470
16

FIG. 47B (1)

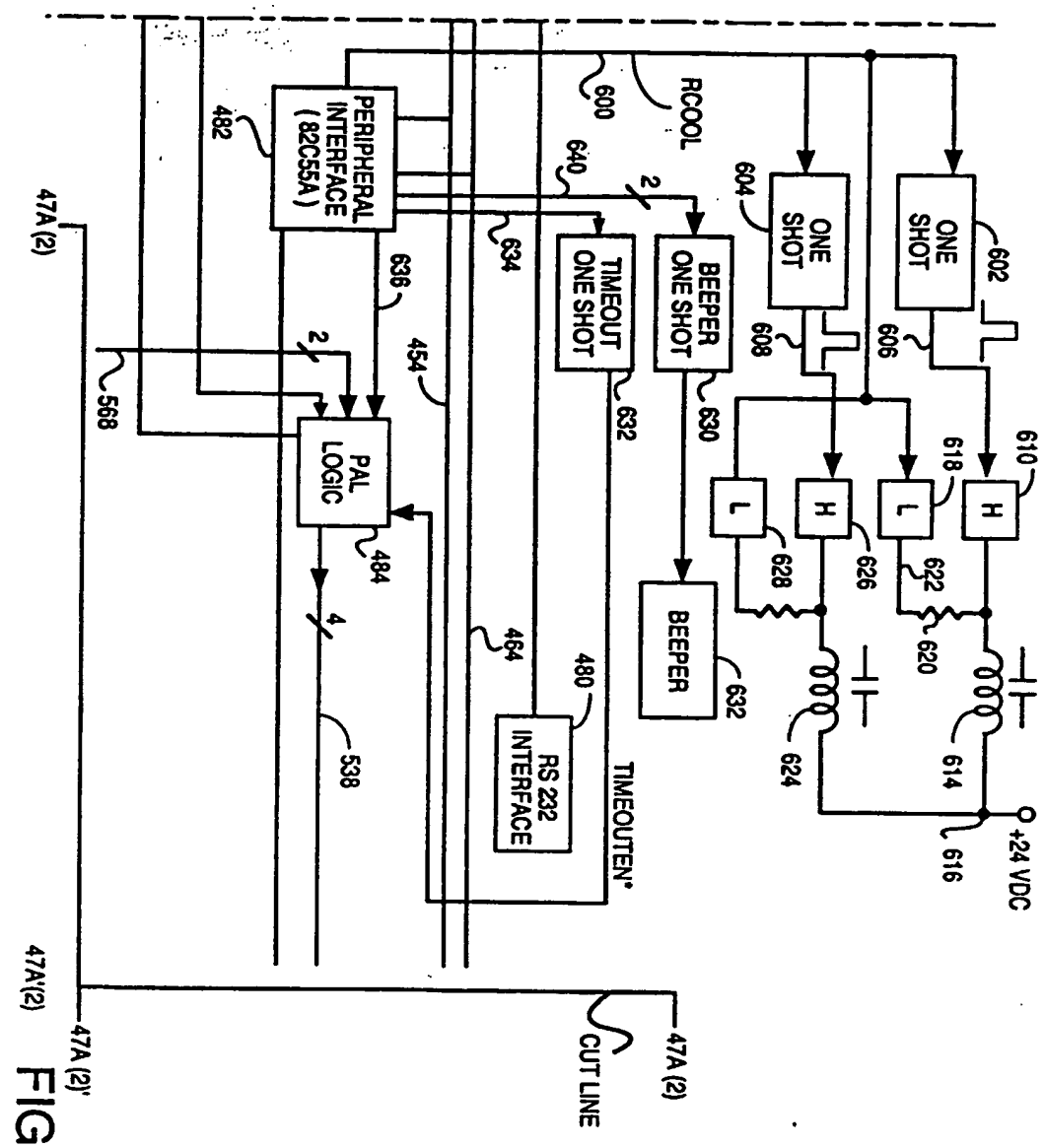

47A (2)
47A'(2)
47A (2)'
PERIPHERAL INTERFACE (82C55A)
482
600
RCOOL
640
634
636
454
568
PAL LOGIC
484
538
TIMEOUT ONE SHOT
632
BEEPER ONE SHOT
630
464
480
RS 232 INTERFACE
TIMEOUTEN*
BEEPER
632
ONE SHOT
604
608
ONE SHOT
602
606
610
618
L
H
L
H
628
626
622
620
624
614
616
+24 VDC
CUT LINE
47A (2)

FIG. 47B (2)

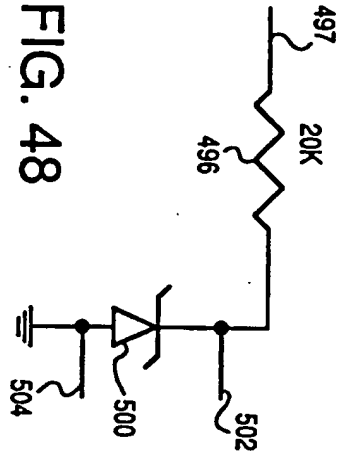

497
20K
496
504
500
502

FIG. 48

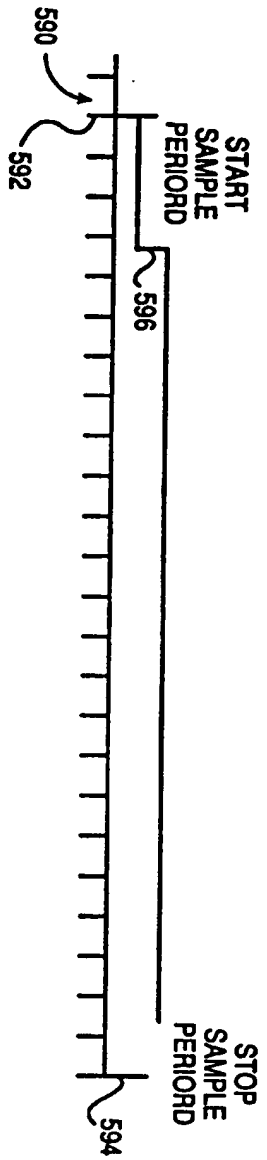

590
592
START SAMPLE PERIORD
596
STOP SAMPLE PERIORD
594

FIG. 49

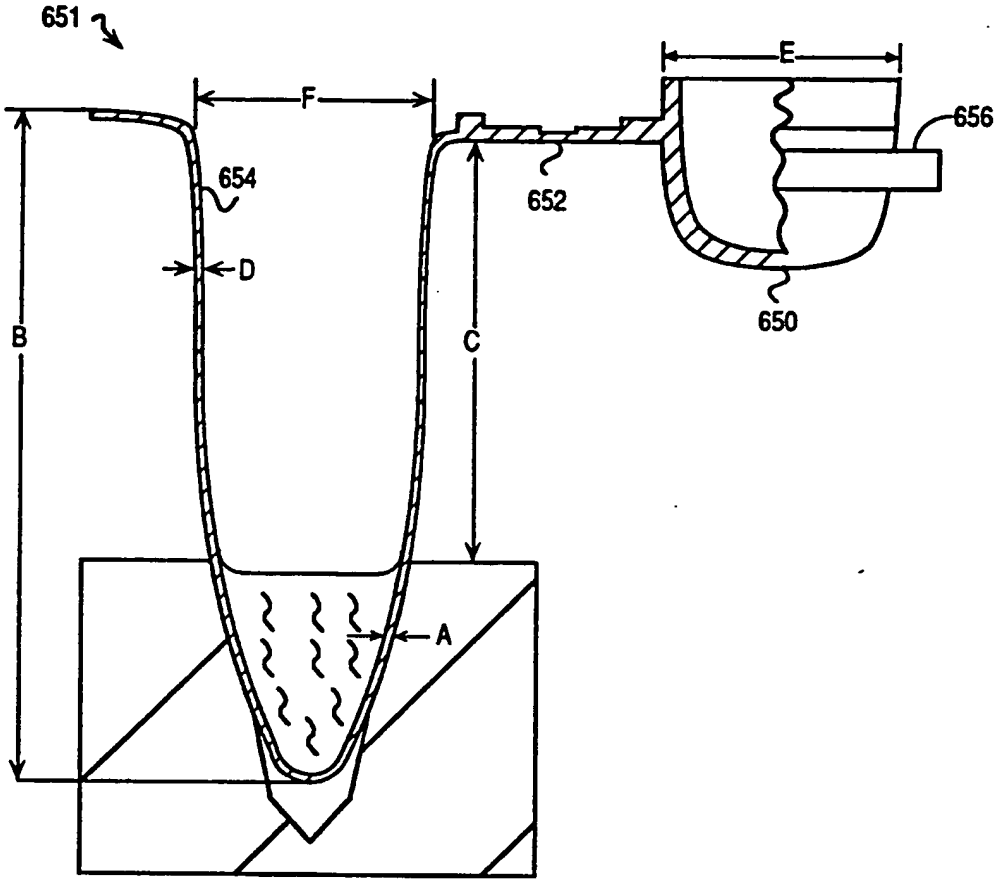


FIG. 50

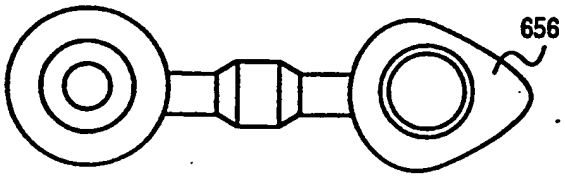


FIG. 52

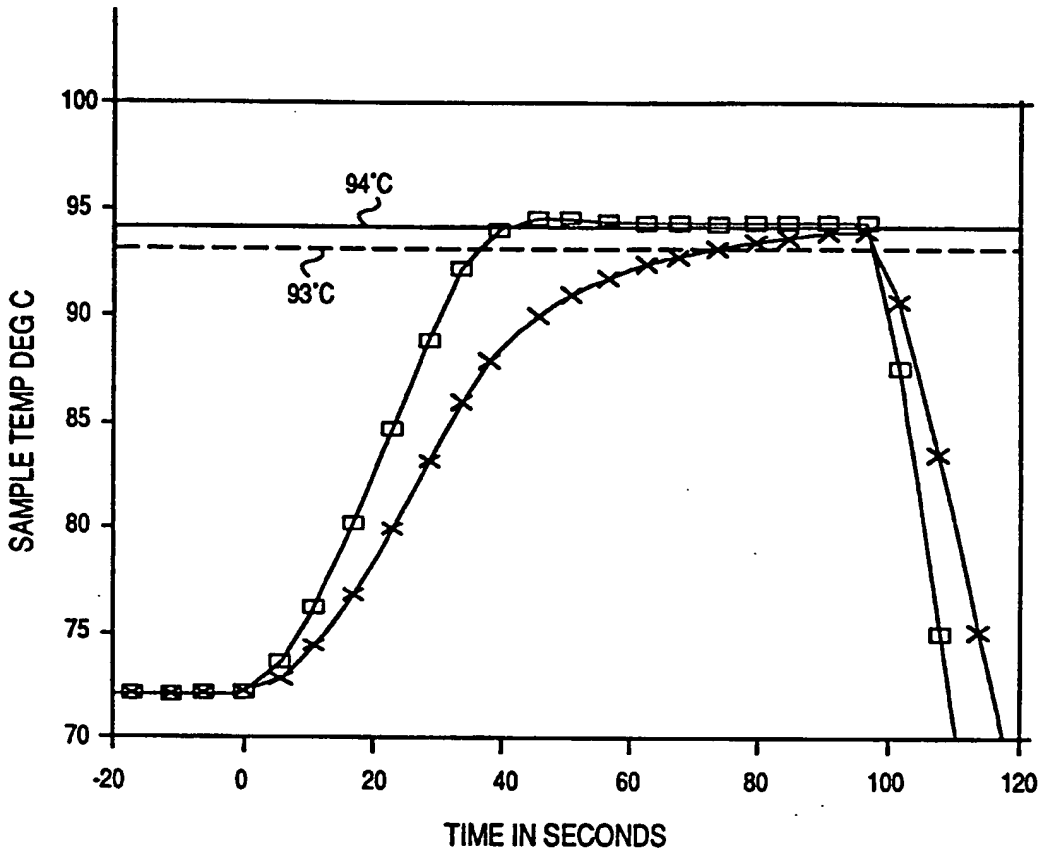

100
95
90
85
80
75
70
94°C
93°C
SAMPLE TEMP DEG C
-20
0
20
40
60
80
100
120
TIME IN SECONDS

FIG. 51

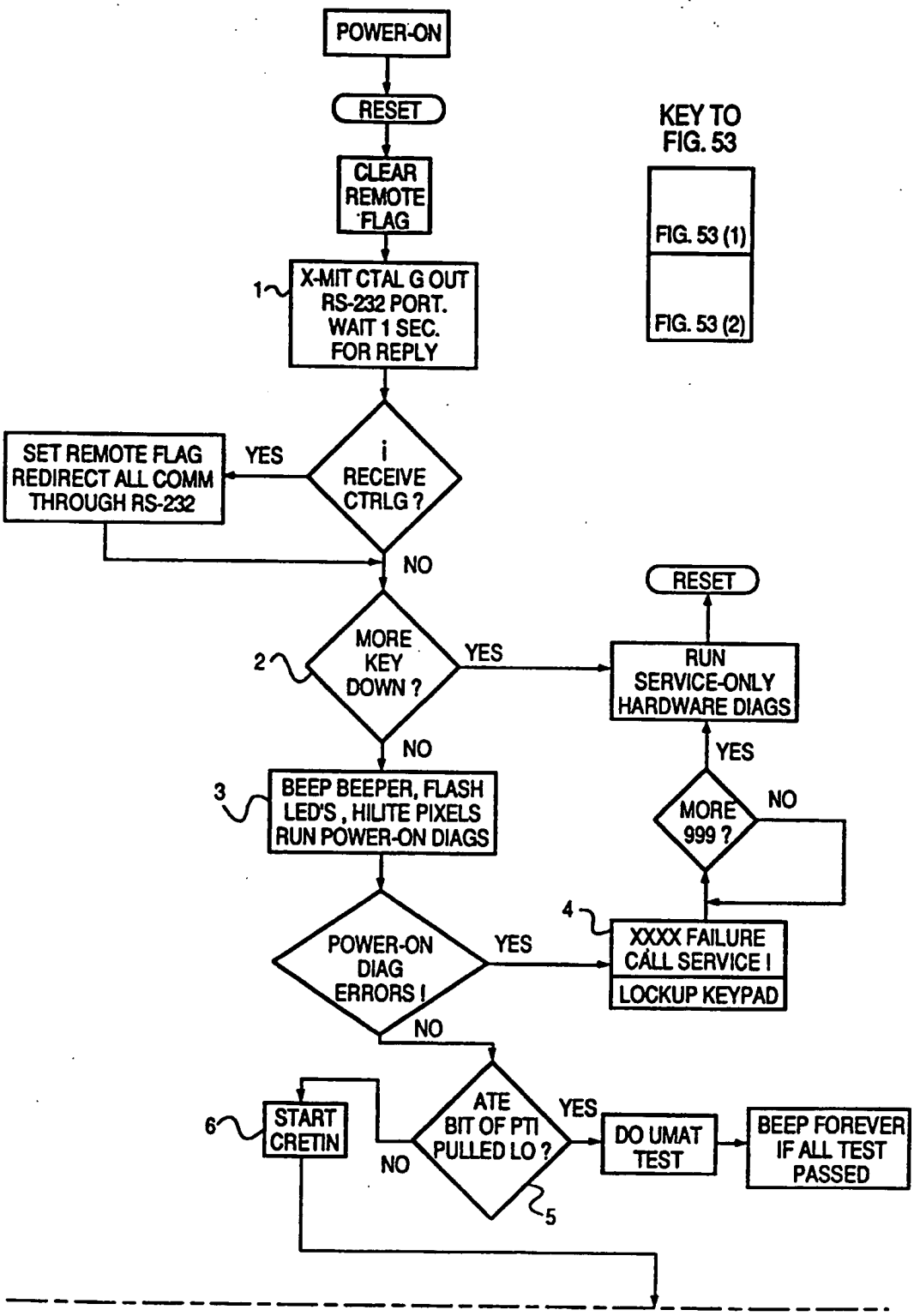

POWER-ON
RESET
CLEAR REMOTE FLAG
1
X-MIT CTAL G OUT RS-232 PORT. WAIT 1 SEC. FOR REPLY
i RECEIVE CTRLG ?
YES
SET REMOTE FLAG REDIRECT ALL COMM THROUGH RS-232
NO
2
MORE KEY DOWN ?
YES
RESET
RUN SERVICE-ONLY HARDWARE DIAGS
YES
NO
MORE 999 ?
NO
3
BEEP BEEPER, FLASH LED'S , HILITE PIXELS RUN POWER-ON DIAGS
4
POWER-ON DIAG ERRORS !
YES
XXXX FAILURE CALL SERVICE !
LOCKUP KEYPAD
NO
6
START CRETIN
ATE BIT OF PTI PULLED LO ?
YES
NO
5
DO UMAT TEST
BEEP FOREVER IF ALL TEST PASSED
KEY TO FIG. 53
FIG. 53 (1)
FIG. 53 (2)

FIG. 53 (1)

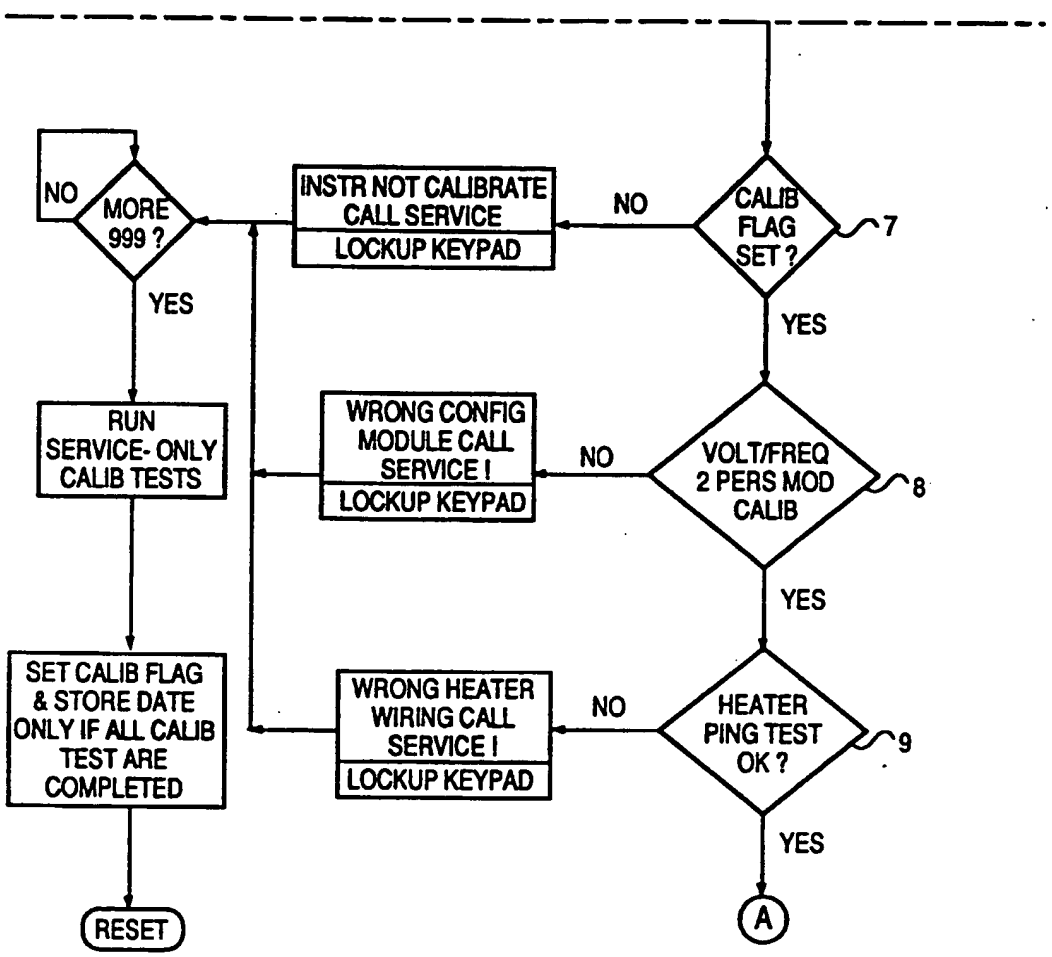

CALIB FLAG SET ?
7
NO
INSTR NOT CALIBRATE CALL SERVICE
LOCKUP KEYPAD
MORE 999 ?
NO
YES
RUN SERVICE- ONLY CALIB TESTS
YES
VOLT/FREQ 2 PERS MOD CALIB
8
NO
WRONG CONFIG MODULE CALL SERVICE !
LOCKUP KEYPAD
YES
HEATER PING TEST OK ?
9
NO
WRONG HEATER WIRING CALL SERVICE !
LOCKUP KEYPAD
YES
A
SET CALIB FLAG & STORE DATE ONLY IF ALL CALIB TEST ARE COMPLETED
RESET

FIG. 53 (2)

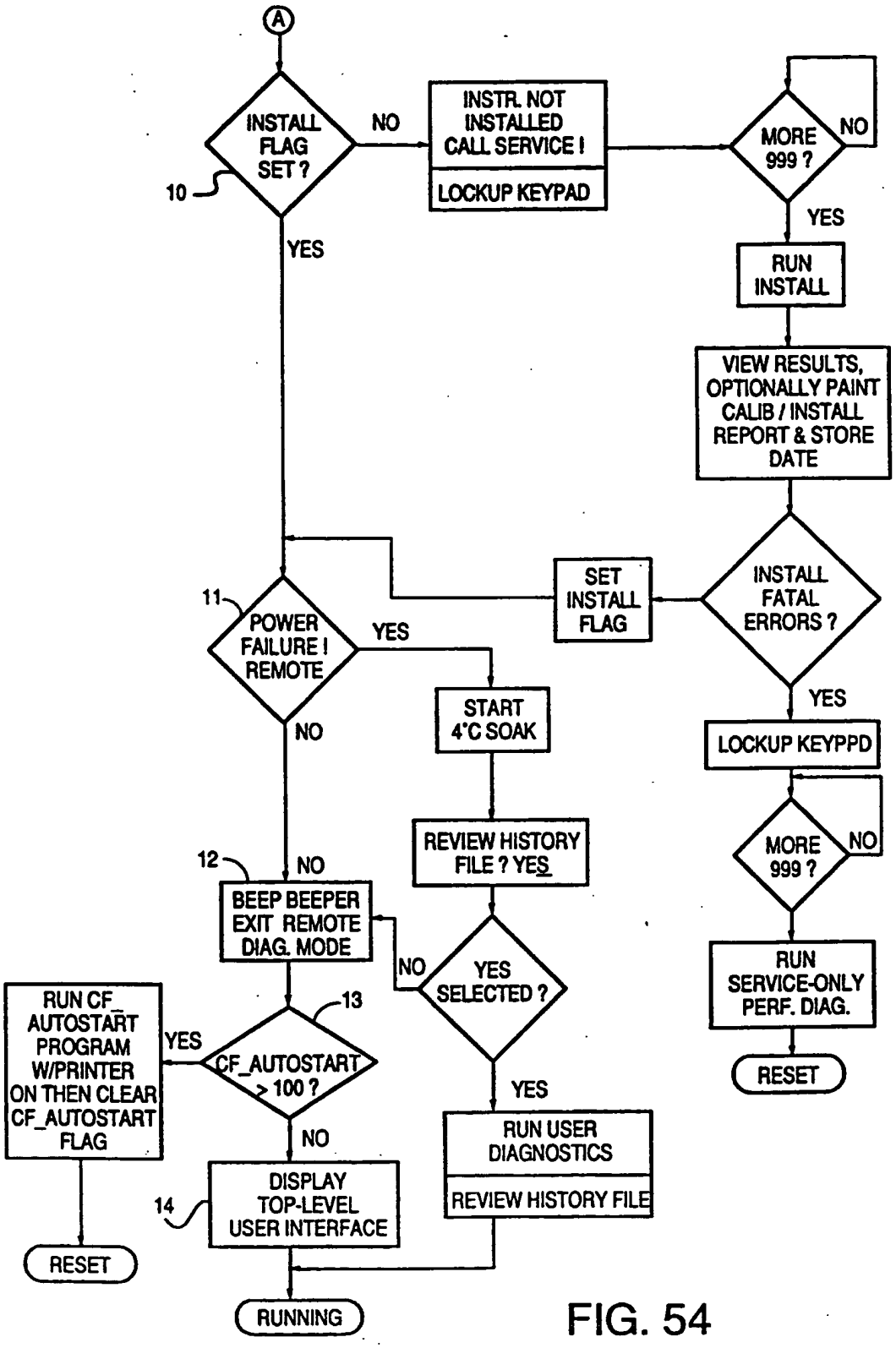

A
INSTALL FLAG SET ?
10
NO
INSTR. NOT INSTALLED CALL SERVICE !
LOCKUP KEYPAD
MORE 999 ?
NO
YES
RUN INSTALL
VIEW RESULTS, OPTIONALLY PAINT CALIB / INSTALL REPORT & STORE DATE
YES
INSTALL FATAL ERRORS ?
SET INSTALL FLAG
11
POWER FAILURE ! REMOTE
YES
NO
START 4°C SOAK
YES
LOCKUP KEYPPD
MORE 999 ?
NO
REVIEW HISTORY FILE ? YES
12
NO
BEEP BEEPER EXIT REMOTE DIAG. MODE
NO
YES SELECTED ?
YES
RUN SERVICE-ONLY PERF. DIAG.
RESET
RUN CF_ AUTOSTART PROGRAM W/PRINTER ON THEN CLEAR CF_AUTOSTART FLAG
YES
13
CF_AUTOSTART > 100 ?
NO
RUN USER DIAGNOSTICS
REVIEW HISTORY FILE
14
DISPLAY TOP-LEVEL USER INTERFACE
RESET
RUNNING

FIG. 54